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DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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OBSTETRICS AND GYNECOLOGY DEVICES PANEL

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July 11, 2014
8:00 a.m.

Food and Drug Administration
White Oak Campus, Building 31
The Great Room, Room 1503
Silver Spring, Maryland

PANEL MEMBERS:

MICHAEL P. DIAMOND, M.D.	Temporary Non-Voting Chair
CHERYL IGLESIA, M.D., FACOG	Non-Voting Member
LISA E. MOORE, M.D., M.S.	Non-Voting Member
PAULA J. HILLARD, M.D.	Non-Voting Member
CRAIG D. SHRIVER, M.D., FACS, COL, MC	Temporary Non-Voting Member
KEITH ISAACSON, M.D.	Temporary Non-Voting Member
ABDELMONEM A. AFIFI, Ph. D.	Temporary Non-Voting Member
CAROL BROWN, M.D.	Temporary Non-Voting Member
DANIEL SIMON, M.D.	Temporary Non-Voting Member
ROBERT F. MATTREY, M.D.	Temporary Non-Voting Member
MICHAEL R. NEUMAN, Ph.D., M.D.	Temporary Non-Voting Member
COLLEEN M. GALLAGHER, Ph.D., M.A.	Temporary Non-Voting Member
MARK A. TALAMINI, M.D.	Temporary Non-Voting Member
RUSSELL R. SNYDER, M.D.	Temporary Non-Voting Member
NICOLAS WENTZENSEN, M.D., Ph.D., M.S.	Temporary Non-Voting Member
KRIS MATTIVI, M.S., PT	Consumer Representative
JAMES GARDNER, M.D., M.B.A.	Industry Representative
DIANE ARONSON	Patient Representative
LCDR S.J. ANDERSON, M.P.H., OCN	Designated Federal Officer

FDA REPRESENTATIVES:

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Director, Division of Reproductive, Gastro-Renal, and Urological Devices
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MORGAN LISCINSKY
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INDUSTRY PRESENTERS:

LORI WARREN, M.D.
LiNA Medical USA

OPEN PUBLIC HEARING SPEAKERS:

JUBILEE BROWN, M.D.
American Association of Gynecologic Laparoscopists (AAGL)
Advancing Minimally Invasive Gynecology

MARC TOGLIA, M.D.
Society of Gynecologic Surgeons (SGS)

ANNA MAZZUCCO, Ph.D.
Cancer Prevention and Treatment Fund (CPTF)

SHARON ANDERSON, M.S.W.
Executive Director
Leiomyosarcoma Direct Research Foundation (LMSdr)

JEFFREY LEVY, M.D.
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Private Citizen

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M E E T I N G

(8:00 a.m.)

DR. DIAMOND: We'd like to go ahead and begin if we could, please. I would like to call this meeting of the Obstetrics and Gynecology Devices Panel of the Medical Devices Advisory Committee to order.

I am Michael Diamond, the Acting Chair of this Panel. I'm Professor and Chair of Obstetrics and Gynecology at Georgia Regents University in Augusta, Georgia. And I'm also the Associate Dean for Research and the Vice President for Clinical and Translational Sciences.

I note for the record that the members present constitute a quorum, as required by 21 C.F.R. Part 14. I would also like to add that Panel members participating in today's meeting have received training in FDA device law and regulations.

For today's agenda, the Panel will discuss issues relevant to the safety of laparoscopic power morcellation devices as it pertains to their potential to disseminate and upstage a confined but undetected or occult uterine malignancy during laparoscopic hysterectomy or myomectomy procedures.

Before we begin, I would like to ask our distinguished Panel members and FDA staff seated at the table to introduce themselves. Please state your name, your area of expertise, your position, and any affiliation.

Mr. Gardner, we'll start with you, if we can, please.

DR. GARDNER: My name is Jim Gardner. I'm a Medical Science Officer and Director of Reimbursement with Cook, Incorporated in Bloomington, Indiana.

MS. MATTIVI: Good morning. Kris Mattivi. I'm the Consumer Representative to the Panel. I'm a physical therapist and a business analyst at WellPoint in Denver.

MS. ARONSON: Good morning. I'm Diane Aronson. I'm a Patient Representative from CDER, the Patient Rep program.

DR. SIMON: I'm Dr. Daniel Simon. I'm the Medical Director at the Vascular Access Center of West Orange in West Orange, New Jersey, and I'm an interventional radiologist by professional training.

DR. GALLAGHER: Colleen Gallagher from the University of Texas MD Anderson Cancer Center. I'm a clinical ethicist. I'm the Chief and Executive Director for the Section of Integrated Ethics in Cancer Care and an Associate Professor in Critical Care.

DR. MATTREY: Robert Mattrey, radiologist, body imager from UC San Diego.

DR. CAROL BROWN: Carol Brown. Good morning. I am a gynecologic oncologist. I'm at Memorial Sloan Kettering Cancer Center, where I'm the Associate Cancer Center Director for Diversity and Outreach, and I'm Associate Professor of OB/GYN at Cornell Weill Medical College.

DR. HILLARD: Paula Hillard, Professor of Obstetrics and

Gynecology, Stanford University School of Medicine.

DR. MOORE: I'm Lisa Moore. I'm a perinatologist at the University of New Mexico in Albuquerque, New Mexico.

DR. IGLESIA: Cheryl Iglesia. I'm a pelvic reconstructive surgeon. I'm the Section Director of Female Pelvic Medicine and Reconstructive Surgery at MedStar Washington Hospital Center, and a Professor of OB/GYN and Urology at Georgetown University School of Medicine.

LCDR ANDERSON: Good morning. Lieutenant Commander Anderson. I'm here to represent the Food and Drug Administration as well as United States Public Health Service. Thank you.

DR. SNYDER: Russell Snyder, OB/GYN at University of Texas Medical Branch in Galveston, where I'm the Division Director of Gynecology.

DR. WENTZENSEN: Nicolas Wentzensen. I'm a Senior Investigator at the National Cancer Institute and working on the epidemiology of gynecologic cancers.

DR. SHRIVER: Good morning. Dr. Craig Shriver, surgical oncologist, Director of the Murtha Cancer Center at Walter Reed National Military Medical Center and Professor of Surgery at Uniformed Services University.

DR. ISAACSON: Keith Isaacson, reproductive endocrinologist at Newton-Wellesley Hospital in Newton, Massachusetts, Associate Professor at

Harvard Medical School.

DR. AFIFI: Abdelmonem Afifi, Professor of Biostatistics at the Fielding School of Public Health at UCLA and former dean of that school.

DR. NEUMAN: Good morning. I'm Michael Neuman, Professor of Biomedical Engineering at Michigan Technological University.

DR. TALAMINI: Morning. My name is Mark Talamini. I'm the Chair of the Department of Surgery at SUNY Stony Brook, and I'm a gastrointestinal surgeon.

DR. FISHER: Good morning. Ben Fisher, Director of the Division of Reproductive, Gastro-Renal, and Neurological Devices within CDRH.

DR. YUSTEIN: Good morning. Ron Yustein, Deputy Director Office of Surveillance and Biometrics, CDRH.

DR. DIAMOND: Members of the audience, if you have not so, please sign the attendance sheets that are located on the registration table directly outside the meeting room. I'd like to take this moment to recognize how complex this issue is. We are grateful to those members of the public who are here to share their thoughts, stories, and perspective. It's critical to our understanding. However, we cannot allow disruptions. Now, we have a lot of work packed into a short amount of time. For the record, there were public disruptions yesterday. As a reminder, if the disruptions continue, we may have to ask you to leave the meeting.

I want to note that the task of the Panel is a scientific panel set

up to make scientific recommendations for this very important public health issue.

Lieutenant Commander Anderson, the Designated Federal Officer for the Obstetrics and Gynecology Device Panel, will now make some introductory remarks.

LCDR ANDERSON: Good morning.

The Food and Drug Administration is convening today's meeting of the OB/GYN Devices Panel of the Medical Devices Advisory Committee under the authority of the Federal Advisory Committee Act (FACA) of 1972. With the exception of the Industry Representative, all members and consultants of the Panel are special Government employees or regular Federal employees from other agencies and are subject to Federal conflict of interest laws and regulations.

The following information on the status of this Panel's compliance with Federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 U.S.C. Section 208 are being provided to participants in today's meeting and to the public.

FDA has determined that members and consultants of this Panel are in compliance with Federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special Government employees and regular Federal employees who have financial conflicts when it is determined that the Agency's need for a

particular individual's services outweighs his or her potential financial conflict of interest.

Related to the discussion of today's meeting, members and consultants of this Panel who are special Government employees or regular Federal employees have been screened for potential financial conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and, for purposes of 18 U.S.C. Section 208, their employees. These interests may include investments; consulting; expert witness testimony; contracts/grants/CRADAs; teaching/speaking/writing; patents and royalties; and primary employment.

For today's agenda, the Panel will continue to discuss issues relevant to the safety of laparoscopic power morcellator devices as it pertains to their potential to disseminate and upstage a confined but undetected occult uterine malignancy during laparoscopic hysterectomy or myomectomy. During the afternoon session, the Panel will be asked to discuss the regulatory classification of laparoscopic power morcellator devices when used to cut and extract tissue during gynecological laparoscopic procedures and to assist FDA in determining the appropriate level of regulatory control necessary for this device type.

Based on the agenda for today's meeting and all financial interests reported by the Panel members and consultants, no conflict of interest waivers have been issued in accordance with 18 U.S.C. Section 208.

James Gardner, M.D., is serving as the Industry Representative, acting on behalf of all related industry, and is employed by Cook, Incorporated.

We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and their exclusion will be noted for the record. FDA encourages all other participants to advise the Panel of any financial relationships that they may have with any firms at issue.

A copy of this statement will be available for review at the registration table during this meeting and will be included as part of the official transcript.

For the duration of the OB/GYN Devices Panel meeting on July 10th to 11th, 2014, Dr. Robert Mattrey has been appointed to serve as temporary non-voting member, and Ms. Diane Aronson has been appointed to serve as temporary non-voting member. For the record, Dr. Mattrey is a member of the Medical Imaging Drugs Advisory Committee in the Center for Drug Evaluation and Research. Ms. Aronson serves as a consultant in the Center for Drug Evaluation and Research. These individuals are special Government employees who have undergone the customary conflict of interest review and have reviewed the material to be considered for this

meeting.

The appointment was authorized by Jill Hartzler Warner, J.D., Associate Commissioner for Special Medical Programs on July 3rd, 2014.

We would like to remind members and consultants that if the discussions involve any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement, and their exclusion will be noted for the record. FDA encourages all other participants to advise the Panel of any financial relationships that they may have with any firms at issue.

Before I turn the meeting back over to Dr. Diamond, I would like to make a few general announcements.

Transcripts of today's meeting will be available from Free State Court Reporting, Incorporated, telephone number 410-974-0947.

Information on purchasing videos of today's meeting and handouts for today's presentations are available at the registration table outside the meeting room.

The press contact for today's meeting is Morgan Liscinsky.

I would like to remind everyone that members of the public and the press are not permitted in the Panel area, which is the area beyond the speaker's podium. I request that reporters please wait to speak to FDA officials until after the Panel has concluded.

If you are presenting in the Open Public Hearing session and have not previously provided an electronic copy of your slide presentation to the FDA, please arrange to do so with Ms. AnnMarie Williams at the registration desk.

In order to help the transcriptionist identify who is speaking, please be sure to identify yourself each and every time you speak, and speak at the microphone.

Finally, please silence your cell phones and other electronic devices at this time.

DR. DIAMOND: We will now recap the day one from the FDA meeting, and I would like to remind public observers at this meeting that while this meeting is open for public observations, public attendees may not participate except at the specific request of the Panel Chair.

Dr. Yustein, you may now begin your opening remarks.

DR. YUSTEIN: Thank you, Dr. Diamond.

Good morning to the members of the Committee and the public who are here today, and thank you for your attendance and participation. I wanted to briefly recap yesterday and set the stage for today.

Yesterday you heard from multiple different stakeholders during the open portion of the meeting, including Ethicon, who reviewed some of the retrospective data they had gathered and evaluated from claims information and their rationale for suspending their global distribution of

their devices. You heard from ACOG regarding their May special report, as well as two patient organizations, the Sarcoma Foundation of America and Fibroid Relief. You heard presentations from Advance Surgical Concepts and Dr. Shibley, who presented information regarding a technique and containment system for morcellation, which is under development, as well as Dr. Elizabeth Pritts, who presented the results of an analysis of the prevalence of unsuspected sarcoma in patients undergoing surgical treatment, quoting a number of 1 in 7,450. And, finally, you heard from numerous individuals whose families have been impacted by the issue we are discussing here this week.

We then had several presentations from FDA-invited speakers, including Dr. Laughlin-Tommaso, who presented background information, speaking to the epidemiology evaluation and nonsurgical treatment of fibroids; Dr. Sobolewski from Duke, who presented information related to different surgical options for fibroid disease; Dr. Ascher from Georgetown University, who presented information on imaging modalities and differentiating malignant from benign lesions with a focus on MRI; and Dr. Cohen from Mount Sinai Hospital, who provided information regarding uterine sarcomas, including stage and treatment options.

You then heard several presentations from FDA summarizing additional data that was contained in your Executive Summary, including the literature review and analysis on the prevalence of unsuspected sarcoma and

its potential impact on patient outcomes which supported our April 2014 Safety Communication.

The Panel spent time on discussion Question No. 1, which related to the quality of the data available to assess the presence of the risk of unsuspected sarcoma and the magnitude of that risk. We heard the Panel's concerns about the quality of the data available for hysterectomy and the lack of data on myomectomy specifically. The Panel noted the differences in the estimates presented by different speakers and the fact that FDA's numbers didn't quite smell right according to the sniff test, although I would like to point out that during ACOG's presentation, they also noted rates of approximately 1 in 500. And during Dr. Sibley's presentation, he also noted 1 case in 200.

The Panel suggested that we revisit our numbers after getting a chance to review Dr. Pritts' data. Some Panel members noted that the number was crucial in order to provide accurate information to patients for decision making, while others on the Panel felt that the exact number was not crucial. The Panel also suggested that FDA collect additional information related to events. The Panel also noted that the risk of upstaging was an important risk to know.

Today we will start the day with an Open Public Hearing similar to yesterday in which you will hear from several individuals and organizations. The remainder of the day will be spent addressing FDA's

questions to the Panel.

Today's questions will focus on three general areas. Number 1: Risk mitigation strategies available, including preoperative, intraoperative, and labeling steps. Regardless of what people believe the quantitative risk is, we need to decide how we can get this risk as close to zero as possible. That's what we'll be asking you to do. Defining the risk and benefit situations based on patient populations. And, third, the need for additional testing, including bench and clinical testing.

As you proceed with your discussion of FDA's questions today, we would like to point out a couple of items. First, FDA recognizes the limitations of available data and agrees that having more quality data is always a good thing. We would always like to be in a better position with better data. But we don't have that data, and that is part of the reason we are here today. Collecting such evidence, even if it's feasible, may take a substantial amount of time. As such, we are asking the Panel to fight through that and provide us with your best recommendations and advice based on the best currently available data as well as your professional and clinical expertise. We recognize that better data may come in the future.

Again, we thank you for all your time and effort in helping us address this issue.

Before concluding, Dr. Diamond, is it okay if Dr. Chris Jones comes up and just answers one question that was asked to us yesterday in

response to a question from Dr. Isaacson?

DR. DIAMOND: Yes, that would be fine.

DR. YUSTEIN: Two minutes. Okay. I'm going to give Dr. Jones a quick two minutes, and then we'll hand it back over.

DR. JONES: Thank you, and good morning. So this question was from Dr. Isaacson when we were doing just questions to the panelists, FDA panelists yesterday. And he asked about in our second part of our analysis looking at impact on outcomes of recurrence, overall survival, disease-free survival, et cetera, were we able to disentangle myomectomy and hysterectomy, and were there myomectomy cases included in the studies that we looked at. And I did not have the number off the top of my head. I felt that the majority were hysterectomy cases, but I wanted to go back and look.

So I looked over the literature last night of those seven studies that were included, and the vast majority are hysterectomy cases. Three of the studies were specific to hysterectomy. However, four of the studies included a mix. And some of them actually broke that down, and I'll give you those particular studies.

So in the Park study that looked at LMS patients, 6 of the 25 patients were myomectomy as their initial surgical procedure. The rest of them were hysterectomy. In the Park study that looked at ESS, 4 of the 23 patients had myomectomy as their initial. And then in the Oduyebo study,

they looked at 21 cases overall, which included LMS and STUMP, so 4 of the 21 were myomectomy. Of the LMS cases, specifically, 2 of 15.

So I just wanted to give you that for your discussion today. Thank you.

DR. DIAMOND: Thank you.

We will now hear from LiNA Medical USA. For the record, LiNA Medical USA is the second of two manufacturers of laparoscopic power morcellators who responded to the *Federal Register* notices call to industry requesting the opportunity to present during the meeting. The information discussed during this section of the meeting should not be considered a representation of all laparoscopic power morcellator manufacturers.

Dr. Lori Warren, you may proceed.

DR. WARREN: Good morning. Good morning, ladies and gentlemen. It's nice to be here. My name is Dr. Lori Warren. I am a gynecologist in Louisville, Kentucky, and I have specialized in minimally invasive surgery. I'm also the Co-Director for the MIGS program at the University of Louisville.

I'm honored to be here today and get to talk about this very important issue. I am here speaking today as a clinical consultant with LiNA Medical. And LiNA is a privately held company based outside of Copenhagen, Denmark. It currently does manufacture a laparoscopic power morcellator.

I want to thank you for arranging this advisory committee

meeting to further explore the topic of morcellation of uterine sarcoma with full involvement of the public, surgeons, GYN societies, and industry. I appreciate the FDA's commitment to raising awareness about this topic, as patient safety is LiNA's number one priority.

In review of the April 17th Safety Communication, FDA's quantitative assessment was focused on an incidence rate of undiagnosed uterine sarcoma in women undergoing treatment for uterine fibroids. A warning was issued about the potential risk of tumor dissemination with power morcellation. We also have concerns about dissemination with other types of morcellation, including hand morcellation.

So alternative treatments were suggested, but associated risks were not reviewed in the Safety Communication, including uterine artery embolization, high-intensity focused ultrasound treatment, abdominal hysterectomy, and vaginal hysterectomy.

So with the ACOG special report that came out, they felt that there was no evidence of catheter-based artery embolization or HIFU that would offer benefit to women with known or occult uterine sarcoma, and the use of these procedures may lead to a delay in diagnosis. This appears to be the case in the LMS deaths that were found after UAE reported in Ihara and Goldberg.

So reviewing morcellation, I feel that this can be often misunderstood or misquoted in the media. When I talk to my patients about

morcellation, I need to really explain that to them. And there's different types of morcellation to be considered. Hand morcellation with a scalpel, that can be done through the abdomen, through an abdominal incision, a mini-laparotomy, or even through the vagina. And with laparoscopic morcellation, which is where we use the power morcellation, it was originally pioneered in the 1980s, and it was a round, tube-like blade that could be spun by hand. In 1993 there was an advancement with Dr. Steiner, and he added a motor creating the very first laparoscopic power morcellator. Today, the concept remains very similar and the same, with just improvements in safety, with safety sheaths and cordless devices.

So we wanted to review some of the data that is available that I wanted to highlight a couple of these studies. In the Park study that was just mentioned, there were 56 patients with Stage I and Stage II LMS, and there was 25 patients in the morcellation group and 31 patients in the non-morcellation group. The results showed higher dissemination rates in the morcellation group, with 44% versus 12.9%, but only one of the 25 patients had had power morcellation. The other 24 patients had actually had hand morcellation via the vagina or through a mini-lap incision.

In the Einstein study looking at LMS patients specifically, there were five patients with the original Stage I LMS, one with hand morcellation. That patient was upstaged to a Stage III, was alive but with disease at 31 months. There were two powered morcellation patients, and one patient

was upstaged to a Stage III with no evidence of disease at 61 months. The additional patient with power morcellation was not upstaged and had no evidence of disease at 30 months. With the two laparotomy supracervical hysterectomy patients, one patient was upstaged to Stage IV and was alive and well but with disease at six months. And the additional patient was not upstaged and had no evidence of disease at 37 months.

In the Morice study, they had 123 uterine sarcoma patients. Thirty-four of those patients received an unspecific mix of hand and power morcellation techniques. And with those results, the rate of pelvic recurrence at six months were not different in either group, 10% versus 10.4%. Overall and disease-free survival were very similar in both groups.

In the Perry study, there were 37 patients with Stage I LMS. In group A, there was a total abdominal hysterectomy without any injury to the uterus. That was 21 patients. In group B, there were patients who underwent procedures involving tumor injury. And then group B, you can see what those procedures were. There was myomectomies done by laparotomy, with half of those patients had recurrences. There was hysteroscopic myomectomies. Three of those four patients recurred. Laparoscopic hysterectomies with morcellation with a knife, meaning more hand morcellation, two had 100% recurrence; sub-total hysterectomy, two out of four. And then, even in abdominal hysterectomies, where the uterus was just injured by a sharp instrument, one of those two patients recurred.

So in reviewing the data, considering this data in conjunction with the data out of the Brigham, it paints a rather inconclusive picture in regards to the risk of tumor injury versus hand morcellation versus power morcellation. Total abdominal hysterectomy without tumor injury may have the lower risk of dissemination, but as we know, it also represents a separate risk profile of that surgical patient, as highlighted by AAGL and ACOG.

In closing, we would love to have a better preoperative test and that's needed, but until that becomes a reality, I think it's important for patients and surgeons to have an informed risk/benefit discussion about the options that are available today.

I want to thank you for letting me speak to you on this topic. And I'd like to urge the Committee to carefully weigh how regulations specific to power morcellation would affect patient care given that apparent risk with the multiple forms of tumor disruption.

Thank you.

DR. DIAMOND: Thank you.

I'd like to thank LiNA Medical USA for their presentation. Do any members of the Panel have any brief clarifying questions?

(No response.)

DR. DIAMOND: I had one. By tumor injury or uterine injury, what did you mean by that?

DR. WARREN: Well, it was happening with just -- even with the

laparotomy, with a myomectomy, just opening up the uterus and shelling the fibroid out was considered tumor injury.

DR. DIAMOND: Okay.

DR. WARREN: And there was tumor injury just with the tenaculum manipulating the uterus that had an underlying sarcoma. And, also, just with anything that would cut in or disrupt the tumor was considered tumor injury in that study.

DR. DIAMOND: Okay. Thank you.

Other questions from the Panel?

(No response.)

DR. WARREN: Okay. Thank you.

DR. DIAMOND: Thank you.

We will now proceed with the Open Public Hearing portion of the meeting. Public attendees are given an opportunity to address the Panel to present data, information, or view relevant to the meeting agenda. Lieutenant Commander Anderson will now read the Open Public Hearing disclosure process statement.

LCDR ANDERSON: Thank you.

Both the Food and Drug Administration and the public believes in a transparent process for information gathering and decision making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the

context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company or a group's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting. Likewise, FDA encourages you at the beginning of your statement to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

DR. DIAMOND: For the record, all Panel members were provided written comments received prior to this meeting. For today's Open Public Hearing, we have received many requests to speak. Each scheduled speaker representing a medical professional society and/or a patient advocacy and research organization will be given eight minutes to address the Panel. Each scheduled speaker who is not representing a medical professional society and/or patient advocacy and research organization will be given five minutes to address the Panel. We ask that you speak clearly to allow the transcriptionist to provide an accurate transcription of the proceedings of the meeting. The Panel appreciates that each speaker will remain cognizant of their speaking time.

The first speaker is Dr. Toglia from the Society of Gynecologic Surgeons. Not seeing Dr. Toglia, we will go on to the next speaker, which is Jubilee Brown from AAGL Advancing Minimally Invasive Gynecology.

(Comments regarding slide setup.)

DR. JUBILEE BROWN: Thank you so much. I do apologize for that.

Thank you so much to the Panel. Thank you for allowing me to present a balanced view of power morcellation.

My name is Jubilee Brown, and I am a gynecologic oncologist at the MD Anderson Cancer Center. Today I represent the AAGL. We are a member organization committed to advancing the care of women through minimally invasive surgery. The AAGL convened a 12-member panel of experts in the field to review all available data, and we have shared that written report with you.

I have no financial relationships nor conflicts to disclose.

Today we will discuss the outcomes from morcellation and the comparative risk of open surgery if morcellation were to be eliminated. Based on these data, we, the AAGL, conclude that for the benefit of women, power morcellation should not be eliminated.

Why is power morcellation important? We have seen a rise in the percentage of surgeries performed through a minimally invasive surgical approach, from about 30% 10 years ago to about 63% in 2012. Technology

such as power morcellation has allowed minimally invasive surgery in 50,000 to 150,000 patients annually. If this is to be eliminated, we will see these converted to open procedures.

Why would that matter? Because we know that morbidity and mortality of open procedures are substantially higher than for minimally invasive surgery. The ACOG special report specifically states that morbidity associated with abdominal hysterectomy is significant, and mortality is increased compared to laparoscopic hysterectomy.

As discussed yesterday, the prevalence of leiomyosarcoma is unclear and ranges somewhere between 1 in 498 and 1 in 7,450. Regardless of the number, the risk is not zero, but is low. The AAGL would caution against eliminating a beneficial technology based on such scant data.

How can we decrease this risk further? Preoperative endometrial biopsy can actually detect 38 to 86% of patients with leiomyosarcoma. This is not perfect, but this fact is often overlooked. And as we heard yesterday, MRI can identify patients with benign fibroids with good predictive value. Advancing age may be a risk. Therefore, appropriate triage may improve safety.

The data on the risk of upstaging are limited, but six reports were available that specifically document leiomyosarcoma. In total, 10 of the 20 patients, or 50%, who went back to surgery after power morcellation were upstaged. A fly in the ointment, however, is the delay from morcellation to

restaging of, as you see, up to 600 days, which really confounds the data.

To Dr. Isaacson's query yesterday regarding laparoscopic myomectomy, three studies shown here with an asterisk included patients who had undergone laparoscopic myomectomy. In total, 2 of 5 patients with laparoscopic myomectomy with power morcellation were upstaged.

But what is the impact of morcellation in the setting of occult leiomyosarcoma? The definitive study has been quoted as Park, who evaluated 56 consecutive patients with presumed Stage I to II leiomyosarcoma. The odds ratio for both recurrence and death were significantly worse for the morcellated group. However, Park did not look specifically at power morcellation, as you've just heard, and included patients who underwent abdominal, vaginal, or laparoscopic morcellation. Also, the odds ratios likely reach statistical significance not because the morcellated patients did worse than expected, but because the non-morcellated patients did better than expected. Compared to any other oncology literature, a recurrence rate like you see here of 23% and death rate of 16% is curiously good. Therefore, we must question the validity of these data.

While George recently found a significantly worse overall survival and progression-free survival rate, and these are, of course, concerning, are these data enough to state with certainty that power morcellation results in worse outcomes and should be banned? We think not.

Leiomyosarcoma is a devastating disease, and we do extend our sympathy to those women who have suffered and to their families. But it is not the only consideration in caring for our patients. A study by Rowe here compared the emotional well-being of subjects before hysterectomy with other medical and psychiatric conditions. Patients with fibroids scored significantly worse than women with hypertension, diabetes, heart disease, and arthritis. Safe and successful treatment of fibroids is important to the quality of life of these women, and we must be careful in considering the rare risk of leiomyosarcoma, which is aggressive with or without morcellation, we do not overlook the impact of uterine fibroids.

And this really brings us to the crux of the matter. Should we eliminate power morcellation solely because of the risk of leiomyosarcoma? Or does the overall risk of morbidity and mortality of open surgery compel us to keep power morcellation and instead minimize the risk?

Using the available literature, we constructed a decision analysis model to examine the risk of leiomyosarcoma in the population who are candidates for power morcellation and compared morbidity and mortality of abdominal hysterectomy compared with laparoscopic hysterectomy with power morcellation. In order to evaluate the worst-case scenario, we conservatively estimated the median prevalence of leiomyosarcoma at 1 in 585. And this corresponds, actually, very closely with the rate of 1 in 498 quoted by the FDA. Also, we varied the risk of local spread due to power

morcellation from 15 to 35%. And we utilized TreeAge Pro 11.0 for the Mac to model comparative risk.

This was, as you see, a complex model in which all variables affecting the decision to proceed with either open or laparoscopic hysterectomy with power morcellation were entered, and all known risks to either procedure were calculated. As you see here, across the board, the morbidity of TLH is less than with an open approach. This is true in this model for all adverse events.

Specifically, the mortality from open hysterectomy is 0.085% while the mortality from the laparoscopic hysterectomy with power morcellation is 0.077%. This yields a difference in favor of laparoscopic hysterectomy with power morcellation even when controlling for all perioperative factors and even when estimating the prevalence at 1 in 585.

Based on these assumptions, this model suggests that the combined mortality from leiomyosarcoma and the potential dissemination through power morcellation would be less than the mortality from open hysterectomy. Converting all hysterectomies currently undergoing power morcellation to open surgery would result in an annual increase of 17 more women dying from surgery each year and a substantial increase in morbidity from open surgery.

Power morcellation is an important tool in treating symptomatic uterine fibroids. It allows up to 150,000 women each year to

undergo minimally invasive surgery when they would otherwise require laparotomy for an abdominal hysterectomy. Can we make the procedure safer? Probably so, through research, education, and improved tissue extraction techniques. We cannot eliminate power morcellation. As the modeling has demonstrated, eliminating power morcellation and converting these women to open hysterectomy would increase mortality from hysterectomy and harm more women. More women each year would die from hysterectomy.

So let us improve but not abandon power morcellation. Our obligation is not only for patients with leiomyosarcoma. It's to all of our patients. We must not sacrifice our patients in an emotional response to a rare event.

Thank you.

DR. DIAMOND: We had started this portion a little bit early, so I just want to see if Dr. Toglia from the Society of Gynecologic Surgeons would like to present.

UNIDENTIFIED SPEAKER: Questions?

DR. DIAMOND: No, we'll do questions after the two.

DR. TOGLIA: Good morning. I apologize for being late. I don't have any slides.

My name is Dr. Mark Toglia. I represent the Society of Gynecologic Surgeons, a medical association that was founded in 1974. SGS

is widely recognized to be a select group of approximately 300 gynecologic surgeons dedicated to the promotion of the highest standards for gynecologic surgical care for women. The mission of the society is to promote excellence in gynecologic surgery through acquisition of knowledge and improvement of skills and the advancement of basic and clinical research, and through both public and professional education.

SGS released a position statement on the topic of power morcellation through its website on May 12th, 2014. The society strongly advocates that gynecologic surgeons communicate clearly with patients regarding the available approaches to hysterectomy, including the risks and benefits for each technique based upon current scientific evidence. The society further advocates that surgeons maintain vigilance with regard to safety when choosing a minimally invasive approach, such as vaginal or laparoscopic hysterectomy.

As you've heard, power morcellation is widely practiced and an accepted technique in minimally invasive gynecologic surgery for hysterectomy. SGS supports and endorses the special report of the American College of Obstetricians and Gynecologists regarding the use of power morcellation and their conclusion that the available evidence and potential benefits of morcellation do not warrant a complete ban of this technique. The society also supports the report of the AAGL task force concerning safe and efficient tissue extraction during hysterectomy, including their statement

that we should have a development of a nationwide prospective registry to accurately -- to collect accurate and reliable data regarding the concerns being presented this week.

Thank you.

DR. DIAMOND: Thank you.

Do members of the Panel have brief clarifying questions of Dr. Toglia or Dr. Brown?

Dr. Brown?

DR. CAROL BROWN: Carol Brown for Dr. Brown, question. In your decision analysis, you compared open -- abdominal hysterectomy to laparoscopic hysterectomy, but did you specifically include or model for patients who would not be able to have a laparoscopic hysterectomy unless they had power morcellation? And if so, how did you do that? So because, you know, there are other options that we've discussed, such as hand morcellation or using a bag or whatever to remove a larger uterus laparoscopically. So how did you build that into your model so that you're clearly comparing just abdominal hysterectomy to laparoscopic hysterectomy with morcellation?

DR. JUBILEE BROWN: So that's a very good question, and thank you for asking that. The one very complicated slide that you couldn't see very well was that decision tree analysis. And we did try and factor that in. It's very difficult to factor in each of those issues. You're correct. At each

decision point, whether it was abdominal versus minimally invasive, whether it was minimally invasive with power morcellation versus other techniques of tissue extraction, we did try and make estimates to the best of our ability based on the available literature for size of fibroids. And I'm happy to provide the Panel with the full manuscript regarding this.

DR. CAROL BROWN: So, just to clarify again, so were you able to isolate the impact of power -- taking away power morcellation by itself, or there are not enough numbers to do that?

DR. JUBILEE BROWN: We included power morcellation as a specific factor. And, in fact, when I said that we varied even the risk of dissemination, that was on top of power morcellation alone. So we did try and factor each of those specific issues in to the best of the literature's ability to support the numbers.

DR. DIAMOND: And Dr. Wentzensen?

DR. WENTZENSEN: Yeah, Nicolas Wentzensen. I have three quick clarifying questions.

First, where did you get your hysterectomy numbers from? You show that there were 63% minimally invasive procedures. We saw much lower numbers yesterday from different sources.

Second question is: What's your mortality estimate that you used in the model for the conventional hysterectomy? Because nobody was willing to give any numbers yesterday, so I'm very curious to hear where you

got that from.

DR. JUBILEE BROWN: Yeah, so the citations actually are on the slides. And so we really combed all of the literature, first of all, to find those data. There are not very many data, as we saw yesterday, with regard to types of hysterectomy. However, in fact, the da Vinci company, Intuitive, has compiled some of their information, and also, with the SEER database and some of the more recent publications, we were able to get that 63% number. Again, I believe the citations are in the slides, so --

DR. WENTZENSEN: And the mortality estimates for conventional hysterectomy?

DR. JUBILEE BROWN: Yeah, so there aren't a lot of data with regard to mortality for either abdominal or laparoscopic hysterectomy. However, again, those citations I'm happy to provide to you. And through the morbidity and mortality estimates in the literature, again, I'll be happy to provide those citations to you.

DR. WENTZENSEN: And who should get MRI before -- I mean, that was another big question --

DR. JUBILEE BROWN: That's a very good question.

DR. WENTZENSEN: That's something you stated as an option, but everybody doesn't seem to make sense --

DR. JUBILEE BROWN: I think based on the information that we heard yesterday, it does look like even conventional MRI, even without

diffusion-weighted technology, may be able to identify patients who are lower risk for this procedure. And based on the pictures that we saw from Dr. Ascher yesterday, images from conventional MRI may be able to show us which patients are lower risk. So it may be that patients with large fibroids who otherwise -- who would require power morcellation should have MRI as part of their workup. But I think to state that definitively would be outside the realm of the data that we have at present.

DR. DIAMOND: Okay. And Dr. Iglesia, Simon, Afifi, and then Aronson, and then we'll move on.

DR. IGLESIA: Okay. Both of you actually mentioned a registry. And, Dr. Brown, I know that in the AAGL statement, they all called for a registry on all uterine treatments, but -- so my question is -- I mean, because that's going to be something that we're going to be asked -- what type of registry do you envision as giving us the most bang for our buck? You know, a device registry may not necessarily be the best because, as you can see, I mean, as you've stated and the speaker before you stated, any time you chop up cancer, unsuspected cancer, you have the potential for a spread, whether it be with the power, hand, vaginally, a knife, et cetera. So are we talking device? Are we talking fibroid? Are we talking a uterine treatment, surgical/nonsurgical? NSQIP has something like that. Or other?

DR. JUBILEE BROWN: So, Dr. Iglesia, I think that's a fantastic question. And I think it's one that we as scientists and researchers will

struggle with, actually, because of resources. You know, clearly, as we've heard yesterday, the ability to kind of backtrack and gain valuable information just from adverse events is really suboptimal. So though it is important to go back -- and hopefully, the FDA can help in gathering more information, as Dr. Brown suggested -- that's probably not going to be adequate to inform all of the questions that we have in order to guide our patients the best.

You know, in the best of all possible worlds, we would emulate Finland, who actually has a full database of all of their patients who have hysterectomy, and they have all the outcomes. And it would be wonderful if we could actually do something like that, where we get comprehensive information. Not only would we have prevalence, but we would know what these procedures end up doing to or for our patients. You know, and I think the AAGL looks to bring together as many groups and institutions, private and public, as possible. But, still, there is certainly room for improvement, and more information is better.

DR. DIAMOND: Dr. Simon?

DR. SIMON: Yes. For Dr. Brown, first, I want to thank you. Your analysis was very helpful to see the juxtaposition of abdominal hysterectomy versus laparoscopic hysterectomy with regard to, ultimately, what the final outcome of mortality is. It was very helpful to sort of see that together.

But I just want to go back to your model. And I was wondering, the mortality ultimately was based on your selecting a figure of 10 to 35%, I think was what you quoted for tumor upstaging?

DR. JUBILEE BROWN: Um-hum.

DR. SIMON: And I'm just wondering, did you guys do -- you know, you end with a -- your conclusion of, you know, we're looking at 17 lives at the end would benefit. But I'm just wondering if you did a tipping point analysis when you did that modeling to understand if you move the needle from 10 to 35 to maybe, let's say like in the Seidman, where they're at 54% tumor upstaging, you know, at what point does it flip, where we are not in favor of abdominal hysterectomy, but now the mortality goes up? Did you do that analysis?

DR. JUBILEE BROWN: Yes. And so, in fact, this is a nice program because it allows you to vary all those different factors, and you can see the prevalence at which -- whether it's prevalence or other outcomes -- but it allowed us to see the prevalence at which it would flip and at which abdominal hysterectomy would have worse outcomes than laparoscopic hysterectomy with power morcellation. Within the range that we are talking about with any of these prevalence numbers that we've heard about yesterday, this model suggests that abdominal hysterectomy has worse outcomes than laparoscopic with power morcellation no matter how you look at the data.

DR. SIMON: So even at a 54 -- if we were -- I happen to like the Seidman article. So even at a 54% upstaging, you're still saying we would have a higher mortality with the abdominal hysterectomy? That's just so I can clarify it --

DR. JUBILEE BROWN: To be -- I don't want to misspeak --

DR. SIMON: Okay.

DR. JUBILEE BROWN: -- and so I don't know how high -- I'd have to look to see how high up we went on upstaging.

DR. SIMON: Okay.

DR. JUBILEE BROWN: But, again, I'm happy to provide you with the full manuscript and any of the data regarding this that you'd like to see.

DR. SIMON: Okay.

DR. DIAMOND: Dr. Afifi?

DR. AFIFI: Abdelmonem Afifi. In your summary slide, you quoted the figure of 1 in 7,450. Is that a figure you arrived at independently, or is that the figure we heard yesterday from Dr. Pritts?

DR. JUBILEE BROWN: Yes, sir, that's the figure we heard yesterday from Dr. Pritts.

DR. AFIFI: Well, I think in another slide, you quoted a figure of 1 in 500-and-something. Was that your own analysis?

DR. JUBILEE BROWN: So I would ask your indulgence in recognizing that we've heard a lot of data here that has modified my

presentation but did not modify the work that we did, the research work that we did in the model. The research work that we did in the model arrived at the number of 1 in 585, which was similar to the FDA's estimate, and that's why we felt comfortable in using that number. That was the number that was used for the model.

DR. AFIFI: Okay. In your introduction, you said you wanted to present a balanced view. Probably a more balanced view would quote all the figures, from 1 in 200 that we heard somewhere up to 1 in 7,450. Thank you.

DR. DIAMOND: Okay. Ms. Aronson?

MS. ARONSON: I, too, was struck by the 17 lives that would have been saved with abdominal surgery versus the power morcellation. Oh, it's --

DR. JUBILEE BROWN: It's the other way around.

MS. ARONSON: So, yes, yes, I'm sorry. Yes. Thank you for clarifying that --

DR. JUBILEE BROWN: So 17 --

MS. ARONSON: So my question was: Would patients that had pretesting have a decision with their physician to be put into abdominal surgery?

DR. JUBILEE BROWN: So I think your question is good. I think that really this model speaks to inform us on how we counsel our patients preoperatively and in how the Panel may make their decision on the

feasibility of continuing power morcellation and what the benefit might be to our patients of continuing that. You know, I think that this model really sort of speaks to the potential increase in risk if we convert patients to open surgery without other good options.

DR. DIAMOND: Thank you.

We're going to now move on to the patient, consumer, and research groups. First is Anna Mazzucco from the Cancer Prevention and Treatment Fund.

DR. MAZZUCCO: Hi, I'm Dr. Anna Mazzucco from the Cancer Prevention and Treatment Fund, so thank you for letting me speak today.

I have a Ph.D. in biology from Harvard Medical School, and I conducted postdoctoral research at the National Cancer Institute, so those are the perspectives I'm speaking from.

I work for a nonprofit organization that conducts research, scrutinizes data and looks at risks and benefits, and tries to explain those to patients and providers. And I should say that the president of our organization is on the Board of Directors for the Alliance for a Stronger FDA, which is a nonprofit dedicated to increasing the resources that the FDA has to be able to do its very important job.

Our organization does not accept funding from any medical device companies, and therefore, I have no conflicts of interest.

We've heard a lot of numbers, so forgive me for saying a few

more. But just to set the stage a little bit, according to the CDC, numbers we heard yesterday as well, there are about 600,000 hysterectomies performed annually in the United States, and at least the numbers I came across yesterday is about 65,000 myomectomies performed annually in the United States.

And from hysterectomies alone, based on the FDA analysis, about 50,000 to 150,000 use power morcellation. And although, obviously, there is a lot of perhaps still continuing discussion today about these numbers, the FDA also estimates that 1 in 350 women potentially undergoing hysterectomy or myomectomy for the treatment of fibroids has an unsuspected uterine sarcoma which could be spread and worsened if a morcellation is used.

And so based on those numbers, I think that does mean that a significant number of women could face the risk of having an undiagnosed malignancy spread each year just from hysterectomy alone. And if we had better numbers for myomectomy, that could be an increased number as well. And I think we've heard yesterday, and as the FDA also stated in their briefing that, unfortunately, at least right now, there is no 100% reliable method to distinguish between fibroids and sarcoma preoperatively.

The estimate of 1 in 350 women having an unsuspected uterine cancer seems much higher than the 1 in 10,000 figure that I came across, which seems to be what's typically quoted to patients. And the FDA has also

estimated in their briefing materials that undiagnosed cancer will be spread or worsened by morcellation in 25 to 65% of cases. And with those numbers, they also quoted an estimated five-year survival as 60% for patients with Stage I disease compared with 22% for those with Stage III or 15% for those with Stage IV.

Obviously, we've also heard a lot over the last day that minimally invasive surgery can offer many advantages to patients, but at least it seemed to me, from the discussion we'd heard so far, that the mortality benefits, specifically mortality, comparing open versus laparoscopic procedures are still a little bit up for debate. But it does seem that it's certain that malignancy spread by morcellation can indeed become a life-threatening situation.

So in light of these findings, we agree with FDA's Safety Communication, that at this time, power morcellators should no longer be used in the removal of uterine fibroids. So the question we're all now left with is whether that warning is sufficient, and is there enough new evidence to suggest altering the Class II classification of these devices and also their current labeling.

So, as we know, power morcellators were originally approved as Class II, moderate risk devices, under the 510(k) process, which does not require clinical trials prior to allowing a device to be marketed. It also does not require inspections to make sure that devices are made and are working

properly, but such inspections are required for prescription drugs, which are approved by the FDA.

Since morcellators were not studied in clinical trials, the risk of undiagnosed sarcoma being disseminated, unfortunately, was not detected prior to their clearance through the 510(k) process. And as a result, patients were harmed by that. And we've heard those stories.

Class III devices are defined as those which pose a significant risk of illness or injury and require clinical testing to establish safety and efficacy. Clearly, we think that power morcellators do meet that definition and should be classified as Class III devices, which would require further clinical studies before they could enter the market again.

Non-clinical performance testing studies, which are done for Class II devices, simply do not seem sufficient to address these safety concerns. If they had been, we might have known several years earlier that morcellators could cause this safety issue.

And I think we all know that everyone agrees more research is needed and that more evidence is needed. Clinical studies are needed to evaluate risk mitigation strategies, such as the use of containment bags. However, as we heard yesterday and the FDA briefing material cites, there are adverse events associated with current specimen bags. For these reasons, bags need to be specifically designed for use of power morcellators, and surgical techniques must also be refined for use with these bags. Clinical

trials are also needed to improve the accuracy of patient diagnostic outcomes when morcellators are used.

As the FDA stated in its summary for today's meeting, the current voluntary reporting system for medical devices is underused and therefore underreports adverse events for all medical devices, including power morcellators, which I think has made some of the data analysis a little bit frustrating.

And as a result, many more patients have died before the risks of morcellation became known, primarily as a result of a physician, whose life was put at risk when a morcellator was used for a uterine fibroid which resulted in Stage IV uterine cancer and additional studies being performed particularly since 2012.

We agree with the American Congress of Obstetricians and Gynecologists that a patient registry should be created to follow patients whose fibroids were previously removed, but that is not enough. And the current FDA warnings we do not think are sufficient either. We need higher standards to ensure that morcellation devices are safe and effective and require clinical trials with sufficient numbers of patients to determine the risks of rare but fatal outcomes, which unfortunately sometimes do occur.

Thank you.

DR. DIAMOND: Thank you.

The next presenter will be Sharon Anderson from the

Leiomyosarcoma Direct Research Foundation.

MS. ANDERSON: Good morning. I'm Sharon Anderson. I'm a social worker and Executive Director of Leiomyosarcoma Direct Research Foundation, also known as LMSdr. I'm also a 12-year Stage IV uterine LMS survivor.

LMS paid for my flight here today to represent patients who have sent me over 40 letters, which I have. Many are on the docket. And many more who just asked me to testify against the use of morcellation for uterine fibroids.

Since 2006 LMSdr has advocated and raised money for LMS research and provide direct patient support. I personally have spent countless hours on the phone and exchanging e-mails with patients. I'm witnessing an alarming increase in the number of women who have had uterine morcellation, which upgrades them to the same risk as a patient, Stage IV.

I'd like to address a few myths. Number one: Uterine LMS is aggressive, and these women would have died within two to five years even without morcellation. The fact is, the majority of uterine LMS women are diagnosed at Stage I, usually at a hysterectomy when they had fibroids. Over 50% of these women never see it again, that is, if they have open abdominal surgery. And there are many long-term survivors of uterine LMS. And it's becoming increasingly more as we get better and better treatments.

Let me introduce you to just a few. These are women who have had open abdominal surgeries for fibroids, which turned out to be, surprise, uterine LMS.

This is Crystal, seven-year survivor, basketball coach and mentor to young women.

Deborah, eight-year survivor. She's a professor of nursing at a major university on the east coast.

Cathy, eight-year survivor. She's the big kid. Lucky grandkids.

Malika, nine years, beautiful.

Laura has survived a decade since diagnosis, and she's here in Washington, D.C.

Theresa, 10-year survivor, and that's a very -- oops, sorry -- Theresa, 10-year survivor, and that's a very lucky dog.

Caroline, she wants you to know she's spent the last 10 years hiking, golfing, and kayaking.

Marsha, 10-year survivor, with her 10 grandchildren, most of who were born after she was diagnosed.

This is one tough cookie. This is Candy. She survived retinoblastoma as an infant, and then she got uterine LMS 11 years ago. She loves going on rides with her husband on their bicycle built for two.

This is Debbie, 11-year survivor. She's ready to go dancing.

Jennifer, 12-year survivor. She's on her dream vacation last

year in Greece.

Myrna, a charming woman living fully in Toronto.

Alison, from Boston, who has a wicked sense of humor, 14 years.

Julie, 16-year survivor. She had an open abdominal surgery at age 16 for myxoid LMS. She's now a radiologist working with cancer patients.

Ilene, 17 years. She's been able to see all her children get through school and go to college.

Brenda, 20 years. She wanted me to let you know how grateful she is for the last two decades of her life.

Helga, she's now 80. She still shows her prized Irish wolfhounds, 20-year survivor.

Joan, 20-year survivor. Lives in California with her family and is a successful realtor.

This is Marge from Pennsylvania, 22-year survivor. She has a huge family, lots of cherished friends, and she told me she is still madly in love with her husband.

And this is my dear friend Beth. She's a 30-year survivor. She had STUMP, of which the last 10 years she has been at Stage IV and fighting.

Now, I've shown you just a few mere survivors. And my question is: What if these women had their cancer morcellated and spewed inside their abdomens? What would have been the impact? How long would

they have survived? Well, let me tell you. Morcellation increases the odds two to four times for abdominal reoccurrences. And these are not just one or two mets in their tummies. These are landslides of painful chemo-resistive tumors. Makes it three times the incidence of death within five years. I'm going to say that again. Three times.

Myth two: Morcellation inside a bag is a good precaution. Morcellation in a bag still compromises the pathologist's ability to find and diagnose uterine LMS. In fact, they can't even tell you what size the tumor was. No diagnosis, no surveillance, no catching a metastasis early to extend survival. In fact, you would be sending them home with a time bomb inside them. And let's face it, bags can break and leak.

Number three: Women should be given a choice whether to have morcellation or an open abdominal surgery. And the fact is no woman ever really wants to elect any chance of dying from cancer, and nor should they be asked to. They trust their doctor knows what's safe. Bad medicine should never be an option. It's criminal to sacrifice one woman in 350 or one woman in 7,000 for the convenience of many others. Hell, it's criminal to sacrifice even one single woman for the convenience of many.

My conclusion: An open abdominal surgery is the safest surgical technique for uterine fibroids, hands down. Ban the use of morcellation to give every woman the best chance of long-term survival and do no harm.

Thank you.

DR. DIAMOND: Thank you.

(Applause.)

DR. DIAMOND: The next speaker is Susan Chaffin from the Association of Cancer Resources. Is Ms. Chaffin here?

(No response.)

DR. DIAMOND: All right. Then the next speaker is Jeffrey Levy from the Institute for Surgical Excellence.

DR. LEVY: Hello. My name is Dr. Jeffrey Levy. I'm representing the Institute for Surgical Excellence, and I want to thank the distinguished Panel for allowing me the chance to speak here today.

My disclosures: I'm a member of the Board of Directors for the Institute of Surgical Excellence and CEO of CaseNetwork. Both organizations have received some educational grants from Intuitive and from the Department of Defense to conduct training and validation studies for the fundamentals of robotic surgery. No activities have related to morcellation, and there are no ties to morcellation companies.

The Institute of Surgical Excellence is a public nonprofit organization dedicated to improving surgical care and patient outcomes. ISE's mission is to support the implementation of safer solutions to complex surgical interventions. We utilize a systems-based approach to bring together key stakeholders. So what we do is we first identify the issues, set

clearly to find goals, facilitate collaboration, assess and fill gaps, develop educational training and assessment tools, and better inform healthcare consumers.

So we have two phases of what we do. One is for the healthcare professional. The other is for the consumer. For the healthcare professional, we promote surgical safety and training standards for those who utilize cutting edge surgical technologies. We help surgeons deliver safe care and improved outcomes. On the patient side, we have activities and resources that promote increased public awareness about data and clinical outcomes related to emerging technologies.

Representing our board of directors include Dr. Martin Martino, Dr. Nazema Y. Siddiqui, and on the right-hand side, you see the surgical advisory board, which has a tremendous diversity of experience and perspective and represent many different societies.

So why are we here? We're here because the decisions that we make in this hearing are decisions that are going to carry an impact on hundreds of thousands of women over the next several years. And we believe that those decisions should be based on the best evidence, involve the best experts, be based on consensus-driven processes, and be inclusive of all stakeholders. And this distinguished group is a tremendous group to help with a lot of the near-term decisions that are made. But I think there are decisions that are going to need to be made after this group leaves after

today.

So one of the problems that we face is that there are multiple position statements from the different societies. Although there's some concurrence with those statements, there are differences in those statements as well. There's a debate about the prevalence, and we've heard about that. There's a lack of agreement on preoperative evaluation. We've heard about that. There is a debate about utility of endoscopic bags. There is no risk stratification tools that are available to us today. There is debate about the value of a registry, and we heard about that again this morning. There are no standards for resident or surgeon training programs for morcellation. And that's one thing that I think is a travesty today.

So the Institute for Surgical Excellence, we believe that we have a unique opportunity and a unique experience to help drive some consensus in these areas. And I'm going to explain how we do it and show some examples of what we've done in the past.

The process begins with bringing together national societies and world experts. We distill their knowledge. We drive consensus. We then determine best practices. We then develop curricula and training models based on those best practices. We deploy and validate curricula and training programs to ensure standardization. We publish our methods and results so others can follow what has been done. And then we provide a continuous improvement model reflecting new evidence as it becomes

available.

I'm going to show a few examples of this and how it's impacted different groups across the country and across the world. The first is a group that some of our board members helped found, and that's a group called ASSET, the Alliance of Surgical Simulation and Education and Training. We brought together key members of senior leadership from surgical societies, accrediting organizations, U.S. military, government, and we worked to establish simulation as a pillar in surgical education, training, performance and assessment.

The goal is to improve the quality and safety of patient care. And we were able to bring together many groups: Almost every major surgical society in America, 28 societies in all, many across the country. We brought together the Department of Defense and Veterans Administration through this process. And one of our first goals was to create a consensus-based framework for the design, validation, and implementation of simulation-based training curricula for surgery. We did that. We published that recently. And now several groups are using that across the world.

And one of the groups that is using it is the Fundamentals of Robotic Surgery. And many of you in the room probably have heard about the efforts that are going on. Our board of directors also has been intricately involved in this process as well. The goal for the FRS was to develop validated multi-specialty technical skills, competency-based curricula for

surgeons to safely and efficiently perform basic robotic-assisted surgeries.

There were grants, as I mentioned earlier, that were received to bring together 100 of the best experts across the world, some of those experts are in the room today, to convene four consensus conferences, one on outcomes measures, two on curriculum development, one on validation criteria, and we just started the validation study. On the right-hand side, you can see the 15 world-class institutions that are participating in that validation study, and they're now validating that curriculum that was developed in this two- to three-year effort. And the next step is to develop high stakes testing exams after we validate the curriculum.

The third example is RTN, the Robotics Training Network, independently again started by the founders of the board for the Institute of Surgical Excellence. They created a group of nine leading institutions that were developing standards as well for resident and fellow training for robotics. And they started off with nine institutions, and then they went to 50 institutions across the country.

Then FRS joined with the Robotic Training Network to create the best of the best, a fundamentals of robotic gynecologic curriculum for surgery, for robotic surgery. And the organizations on the right, including all of the major organizations in the field of OB/GYN, were included. The president of the AMA was participating in this as well, and JCAHO participated in this meeting, too.

So where do we go from here? We believe that if we can conduct an expert consensus conference or multiple conferences, we can address over the long term many of the issues that have been discussed today. ISE would like to help organize and facilitate that process. And we believe that we can have a positive impact on hundreds of thousands of women over the next several years. We believe that through this process, we can have a unified society position, we can have agreed-upon prevalence, we can have standardized patient consents, we can have risk stratification tools, and we can even standardize resident and surgeon training.

Thank you.

DR. DIAMOND: Thank you.

Has Susan Chaffin arrived, or is there another representative of the Association of Cancer Resources?

(No response.)

DR. DIAMOND: All right. If not, are there any brief clarifying questions from the Panel for Dr. Mazzucco, Ms. Anderson, or Dr. Levy?

(No response.)

DR. DIAMOND: Okay. Seeing none -- oh, I'm sorry. There is one. Dr. Brown?

DR. CAROL BROWN: I just had a clarifying question for the last speaker. So does ISE have a specific position on the use -- I heard you state that you're calling for a conference, but do you have a specific position on the

use of power morcellators?

DR. LEVY: We do not. And the goal of ISE is to be a convener of the experts and to provide the process to get to the endpoints. But we are not the experts, and we are not providing the position statement.

DR. DIAMOND: All right. We will then move on to individual presentations. First is Dr. Hoonan -- I apologize -- Noorchashm, who will presenting and also will have a one-minute video presentation.

DR. NOORCHASHM: My name is Hoonan Noorchashm. I have the very great displeasure of being here today as husband to Dr. Amy Josephine Reed. I'm accompanied here with two of my children, two out of six, and I'm standing before you as a general and cardiothoracic surgeon. Before I proceed with my presentation to you, I think it's very important for everyone in this room, all non-gynecologists to see what this procedure actually is. I don't think any one of these distinguished gynecological leaders sitting in this room have had the courage to actually show what this procedure is and what it does to people.

This is a public domain video available on YouTube and accessed through the FDA's Internet. I don't know why it's not playing.

(Pause.)

DR. NOORCHASHM: Well, what I can do is I can proceed with my verbal commentary and my PowerPoint presentation, and then maybe Derrick could fix this problem and we can come back to it.

Derrick, is my PowerPoint presentation at least available? And this is, you know --

(Pause.)

DR. NOORCHASHM: As I said, I'm standing before you as husband to my wife, Dr. Amy Josephine Reed, father of six, two of my children are here. I'm a general surgeon trained at Penn. I'm a cardiothoracic surgeon trained at the Brigham and Women's Hospital.

I am absolutely astonished by the majority of this expert Panel sitting before me, the gynecological surgeons, who really appear to be thinking that an iatrogenic epidemic of Stage IV cancer was just discovered in December of 2013, 20 years after, 20 years after your device has been put on the market.

You know, I say to you, Dr. Isaacson, take a good look at yourself. Who exactly do you think should have been reporting these complications back to the FDA? Your patients? Well, we did in December of 2013, sir.

And now, incredibly, you all sit here claiming that this is fabricated, that there is a shadow of doubt as to what this is. I hope we can pull up this video for everyone to see.

Dr. Isaacson, why was Erica Kaitz within Partners Health System subjected to this oncological complication and then subsequently died at your home institution of Partners Health in Boston? And this was not

reported to the FDA. Hell, it wasn't even reported as a sentinel safety event within Partners Health. Perhaps her upstaging was also fabricated? Perhaps her upstaging did not happen? Your specialty's negligent thinking is intolerable. But the general surgeons on this Committee know better. Dr. Shriver, Dr. Talamini, you do know better.

This is a systemic practice. It's not safe. It's not responsible. And if you don't speak up now, you have done a great wrong. Colonel Shriver, it's your duty to protect the public from this not only as a surgeon but as an officer in the United States military. This is not some foreign enemy. This is a group of surgeons committing industry-wide negligence.

Mincing up tumors with malignant potential inside a woman's body is a massive corruption of surgical technique. The mainstay of surgical therapy of sarcomas is en bloc resection with good margins. That is basic surgery. Gynecologists have corrupted that.

Dr. Shriver, they're saying that this morcellation is for the benefit of the majority. I ask you: Where in our country, where in this society have we accepted the sacrifice of a minority subset of women for the benefit of the majority, and what is that number that we're going to accept? 1 in 350? Is it 1 in 1,000? Is it 1 in 500? Especially when it's avoidable.

Dr. Talamini, they say that this should be a matter of women's choice. Bad medicine. Is bad medicine a matter of choice? Should we offer

our patients this procedure?

You see, these surgeons have built this device and trained a whole generation of surgeons to mince up tissues inside of women's bodies. I ask you, is this a safe and logical device? Is this something you want your own mother or sister or wife or daughter to be subject to? I hope I can show you the video. The only categorization this device requires now is banned, unsafe, illogical, incorrect, unacceptable, and deadly. How sickening, how sickening that these gynecologists are incapable of seeing what they do. It is collective blindness. It has happened in history before. You don't have to go back too far in history to see that whole groups of people could be blind to a fundamental error in judgment.

Now, these 30 women up there, they are real. That's your reporting. You want to go confirm that? The *Wall Street Journal* confirmed that. They published the collage. They went and talked to individual women, looked at their records. These women are real. There they are. Look at them. Erica Kaitz, Danusia Bennett-Taber, Patricia Daley, Sandra Brown, Mary Alice Martin Dolin (ph.), Nancy Lincoln Davies, Barbara Leary, Margie Miller, Elizabeth Jacobson, Laurie Kaufman, Jenny Profer (ph.), all dead from upstaging, from upstaging of their cancers using an avoidable technique, using an avoidable device. You cannot allow this to go on. You cannot.

The gynecologists who don't see this are poorly trained, are not thinking straight, and they don't see the devastation they cause. They call

this for the benefit of the majority. I indeed ask you would you want yourself, your mother, your sister, your daughter to be subject to this. Now, I hope that Derrick has fixed this problem for me and can play this video because none of you had the courage to show it. All of you, all of you talk statistics, but none of you had the courage to show what this is. You don't have to go to medical school to get this.

(Video played.)

DR. NOORCHASHM: That's a morcellator. That's a uterus being morcellated. It fell into the peritoneal cavity. If there's sarcoma in there, it'll spread. This is not correct. This is dangerous. This is a public health hazard. This cannot go on. This was done to my wife, and it was done to all those people in that picture. You want to go confirm this? Feel free. Confirm. Shame on you all. You are not doctors.

(Applause.)

DR. DIAMOND: The next speaker is Dr. Amy Reed.

DR. REED: Hello. My name is Amy Reed. I was going to give a presentation today on my personal experience with morcellation as a physician. I have my M.D. and Ph.D. from the University of Pennsylvania where I completed my anesthesiology residency and critical care fellowship. I'm dual-board certified, and I am a practitioner at Harvard Medical School's teaching hospital, Beth Israel Deaconess Medical Center. But I scrapped my entire presentation last night because the Panel's discussion point at the end

of yesterday left me with the feeling as though that the impetus for this gathering is to protect the practice of morcellation, how can we make morcellation safer, how can we protect the safety of morcellation, but what about protecting the patient? The reason I say that is that not one of you ever brought up the question, well, should we just stop, should we stop using these before we can address these questions, which I think is pretty basic.

So I'm going to say that's a resounding yes, we should stop using them, and the reason why is because morcellators are a failure. They are a failure of device safety, of medical self-regulation, and finally, of federal regulation.

So my video is embedded, and I do want to show you, if possible, or not -- you get the point. I don't need to. I'm short on time anyhow.

Morcellation causes dripping into the peritoneal cavity, blood, tissue, fragments. You pull the distorted pathological specimen. You go from a nice round uterus to a shred of tissue with drippings as you're pulling it out. So I ask you, does this pass the sniff test? Perhaps we should ask people outside of medicine: Is this good? Is this good practice? If you ask your son to clean something up off the floor and he did it in that manner, would you say good job, why don't we do that again?

Morcellation is bad medicine. As Dr. Shriver said yesterday, when you morcellate a specimen, pieces are left behind, large, small. The

ACOG wants to train its surgeons to pick up fragments, go right ahead, but there's microscopic disease you cannot see, benign/cancerous tissue; both can seed the peritoneum, both can lead to complications, both are bad practice.

Morcellation interferes with pathological diagnosis. This leads to misdiagnoses. We talked briefly about dissemination of myomas in the peritoneal cavity prior to the advent of laparoscopic surgery. But I ask you: Did you miss diagnoses of malignancy, Dr. Isaacson? Have you ever heard of that because you morcellated a myoma in an open cavity? No. That would be considered poor surgical technique.

We heard a lot about bags. We heard from people who studied bags, people who make bags, people who sell bags. Do bags address this issue of morcellation? Absolutely not. We will still miss diagnoses with bags. Forget the tearing and the rupturing and numbers that we can waste more time debating.

So why do we use these terrible things? Why are we fighting to protect these? Well, now we turn to why these are a failure of medical self-regulation. And we've heard a lot about risk. We heard this morning about risk. Yesterday, Dr. Lawrence from the ACOG talked about we must be careful that we don't trade one risk for another.

So let's talk about the risk exactly that we are trading because a lot of people, and it was said this morning, if you don't morcellate, then can

we do this laparoscopically? And for a lot of GYNs, the answer is apparently no, you can't. We are taking away laparoscopes out of GYNs' hands if we say you cannot morcellate. It's been said over and over.

Is this true? No. Laparoscopic surgery is surgery through small incisions. Morcellation is shredding up tissue. They are distinct. Other branches of surgery, thoracic, general surgical oncologists, breast surgeons all operate laparoscopically without morcellation. So how do they do this wondrous feat? They make an incision appropriate for the mass in question. Let me repeat myself. They make an incision appropriate for the mass in question. If I took my daughter, 15, to a breast surgeon, and I said to the breast surgeon -- and I said my daughter has a 3 cm mass in her breast, the SEER registry says she has a 1 in 571,000 chance of having breast cancer, so I don't want you to take it out, just mince it up a little bit aesthetically, but I don't want it biopsied in a way that could give me a tissue diagnosis, I hope someone would commit me.

So let's talk about the actual risk that these people have because they've gotten wide open abdominal hysterectomies. Let's pretend there are no middle options. There are no mini-laparotomy incisions. Let's pretend all GYNs either do it morcellating or a full abdominal hysterectomy.

There are women who will say I left the hospital two days later than I had planned. I was on the couch 10 days more than I had expected.

Erica Kaitz, my husband presented, died in the hospital 18

agonizing months after morcellation led to disseminated peritoneal sarcoma. This sarcoma grew through her port site. I lost extra blood, 40 cc's, statistically significant more blood was lost, half a tube of toothpaste. I had fever from my incision. Sure, absolutely. I starved to death. Morcellator caused peritoneal sarcomatosis.

Patricia Daley. I had to take a week of antibiotics for infection. I was on Kefzol. I had a little bit of inflammation.

Meredith Hammond has to take six months of chemotherapy to hopefully counter the morcellation that she had that would have otherwise been Stage I uterine leiomyosarcoma. She lost her hair and woke up vomiting from the drugs.

And worst-case scenario, I had to have surgery, I had to have another surgery to fix my wound because it didn't heal. It got infected. I didn't want this big incision, but you forced my hand because you took away morcellators. Were you left with something like mine?

So tell me: How do we weigh these decisions? What numbers? What point system can we use to balance? Maybe we can waste another day or two arguing whether it's 1 in 400 or 1 in 7,000 because, as we heard from Dr. Isaacson, he wants to inform his patients to the exact number that'll make a difference, because informed consent does not protect patients. Counseling does not protect patients. Patient physician dialogue does not protect patients. It protects gynecological surgeons from legal culpability of

an action that is completely avoidable.

DR. DIAMOND: Please sum up.

DR. REED: Yes. The only thing I want to say is why this is a federal regulation. Over half of the physicians on the board and invited speakers are gynecologists, five of whom are in positions of power. I ask you why did none of you report the complications? Did you not consider the FDA worthy of hearing of these complications, or did you not consider us complications?

Surgical [sic] of Gynecological Oncology and past president, Dr. Cohen, why were we never reported? I call for the FDA to use common sense. Ask people outside of this specialty. Do not rely on gynecologists to make an informed decision on this. Do not allow them to inform your decision. Recuse them from this board and hold them personally, if not potentially criminally, liable for what you've done to me and these women.

(Applause.)

LCDR ANDERSON: I'd like to make the announcement --

DR. DIAMOND: Okay. We're going to take a ten-minute break.

(Off the record.)

(On the record.)

DR. DIAMOND: We'll go ahead and resume the Panel meeting. The next speaker is Gene Manley.

MR. MANLEY: I've put this up on the -- hello, my name is

Gene Manley. I do not have any financial interests to declare.

Ladies and gentlemen, thank you for this opportunity to speak today. My niece is Brenda Leuzzi, and she is dying of Stage IV, inoperable uterine leiomyosarcoma. Twenty-two months ago, my niece had minimally invasive surgery for fibroids, which was accomplished by using a morcellator as the extraction method. Brenda was scared of cancer and was tested repeatedly, and even delayed surgery one day to receive the results of the final test and was assured that she did not have cancer. This was at the University of Rochester Medical School. I believe it has some pretty good testing there, so this is in Rochester, New York.

Retrospectively, what my family has learned, preoperatively, there is not any reliable techniques to differentiate between ULMS and fibroids. If there were, they'd have found them.

The stated rate for occulent [sic] sarcoma in supposed benign fibroids is grossly understated, if stated at all. The studies the FDA used in their key findings of April 17th, 2014 shows a 1 in 350 for occulent sarcoma. Using Rochester, New York, in Rochester, New York -- and I believe one of the gentlemen here wanted to have numbers that showed a whole bunch of things. Please look at the study on the screen.

So if we go down here just a little bit, this is the number of robotic cases, the 10 highest in the state of New York, okay? Two Rochester Hospitals are on that. The reason I did that, picked the robotics, is because

we can all agree that if you do a hysterectomy robotically, right, you're probably going to morcellate. I don't even want to use the -- all of that number, right, because if you go to this page right here, in all of New York state, they had 22,073 hysterectomies; 41% were for fibroid disease, okay, 41%.

That doesn't help Rochester. In Rochester, New York, 58% of 1,245 is what they do robotically. 41% of that, right, is 510. So that takes the bottom four of the top five. So it takes the uterine sarcomas out, it takes all of the sarcomas out, they think are all of the uterine cancers that they can find, prolapse. All it is is fibroids, right?

So the numbers are about the same. You take that by -- if you take it back two years, you take it up two years, the number is very close because they've had three, three people that had uterine leiomyosarcoma morcellated in their cavity in the last 60 months. Three. I have talked to too many sarcoma specialists at sarcoma centers and surgeons, and they say same thing as the colonel. You drop a piece of blood, and this thing is going to grow, the reason my niece is dying. So I'm begging guys like him to see if they can save her life. And they say there's no saving. The saving should have happened 22 months ago when they disseminated this tumor that they didn't know what it was. I've talked to Sugarbaker, Kane, Khushalani, and I'm begging for a miracle. If I knew his name -- e-mail and address, I'd be doing him, too, okay?

So don't sit here and tell me that this is -- that sarcoma, morcellated sarcoma does not have consequences. All of you gentlemen know it, all of you gentlemen and ladies know it. If you knew they had sarcoma, uterine sarcoma, you wouldn't do it, so since you don't know, you can't do it.

Thank you.

DR. DIAMOND: Thank you.

(Applause.)

DR. DIAMOND: The next speaker is Michael Paasche-Orlow.

DR. PAASCHE-ORLOW: Hi, my name is Michael Paasche-Orlow. Thank you for letting me present today. I have no conflicts of interest to declare. Actually, I would like to share with you that I serve as a voting member of the FDA NDAC Panel. I usually sit in that corner over there.

The three topics I want to cover regarding LPM, laparoscopic power morcellator, one is prevalence, and I hope to share new evidence with you about unanticipated cancer being much more common than expected. The second thing is about harm. I hold that there is significant morbidity and mortality. I can share some new evidence about this as well. And the third is about the risk/benefit profile when compared to alternatives. And I hope to convince you, please, that when considering these three things, that really laparoscopic power morcellators should be removed from the market.

Now, about the risk/benefit ratio. The first thing is that there

are multiple alternatives. And when you listen to presentations about conceptual models or decision trees by people like Jubilee Brown, you have to say why are you comparing this to an open procedure? In fact, most people would not need an open procedure. The second thing about that is that LPM is simply not necessary.

Now, there was a theory that minimally invasive supracervical hysterectomies facilitated by an LPM should be done to retain the cervix because it would be beneficial for sexual health. This theory had been debunked. There is no reason to retain the cervix. There's also been gross misunderstanding and misuse of the Wiser paper and data from the HCUP dataset. It's in the packet, and I think that this issue about mortality from the Wiser paper has been presented and talked about. So there are several things about this paper that I think are grossly misunderstood.

It's been used to cite a three times odds ratio for increased higher rate of death from abdominal hysterectomy versus laparoscopic hysterectomy. So, first of all, the paper does not purport or try to differentiate amongst various types of laparoscopic hysterectomies. It's a total mix of all the different types of hysterectomies in the laparoscopic side. So it's nothing to do with power morcellation versus open. Just a misunderstanding of the paper.

The second thing about this paper is it does not -- the odds ratio of three times is an unadjusted odds ratio. Look at the bottom of

table 2. The adjusted odds ratio in that paper is .69 with a 95% confidence interval that crosses 1. That means that in that paper, it is not a statistically significant difference in mortality. Look at the paper.

The next thing about that paper that really should be questioned is about the way they did adjustment. So they actually did a good job to try to do the adjustment odds ratio. But if you look carefully at the methods, they included in the adjustment status procedural elective status. That means that the dataset includes non-elective procedures. That mixes apples and oranges when you think about mortality. If you include non-elective open hysterectomies in the conversation, then it's unfair to make conversation about mortality. Non-elective procedures versus elective procedures, different buckets, not done in this paper.

The next thing is that when you talk about relative risk ratios, you always have to ask yourself, well, what's the absolute risk. And the absolute risk in this paper is exclusively with respect to perioperative death, and the absolute risks are up there, between 1 and, you know, 3,200 and 1 in 8,500 or 7. But, of course, this does not include subsequent death from recurrent cancer.

With respect to harm, in the packet -- and it has been discussed, data presented by George and Park. I want to mention that I've been in personal communication with two other investigators: Ian Judson from Great Britain, he has a cohort of over 200 sarcoma patients now; his

data will be coming out, and I can share a little bit of that that he's shared with me in private communication. And also Dr. Holgenberger (ph.), who's got a cohort that's going to be presented from Germany.

This is some time to recurrence. The black line is people who had open hysterectomies. The blue and red lines are people who had various types of morcellation in different contexts. And the green line are people who had palliative procedures. And these are all massively statistically significant.

Now, with respect to prevalence, I've used MarketScan data -- now, there's been a proposal to create a prospective registry. This is a bad idea. We can use historic data. But you have to be very careful about how you include historic data. You can't just grab papers off the shelf all the way back from 1960 thinking that you can use things from irrelevant sources. I've brought together MarketScan data. This is claims encounters. These datasets -- for now, I'm going to present very rapidly data I have from over 19,000 laparoscopic supracervical hysterectomies from 2007 and 2012.

In this dataset, I have found -- I have adjudicated and confirmed with blinded adjudicators cancer post-procedure rates of uterine cancers to a rate of 1 in 481. If you add endometrial hyperplasia, which does not have the same death rate, but you've done no favor to these women by spreading their hyperplastic cells, that gets to a rate of 1 in 334. And if you add adnexal cancers, because you also end up morcellating some ovarian

cancers by accident, you end up with a rate of 1 in 231 cancers spread in these over 19,000 laparoscopic supracervical hysterectomies. Prior to sending this out, I'm going to have a whole new set of other external adjudicators to rate each of these cases.

DR. DIAMOND: Please wrap up.

DR. PAASCHE-ORLOW: Based on the prevalence, harm, and the alternatives, I really strongly recommend that you remove laparoscopic power morcellators from the market until and unless there is a proof and safe manner to use these devices.

Thank you.

(Applause.)

DR. DIAMOND: Thank you.

The next speaker will be Sean Griffith.

MR. GRIFFITH: Thank you. My name is Sean Griffith. I have no financial interest in this. I am the brother-in-law of Dr. Hoonan Noorchashm and the brother-in-law of Dr. Amy Reed.

I'm here to read a letter that is part of the docket already, but I would like to make it part of the oral record at the hearing.

It is a letter from Jon Morris, who is a doctor, a professor, and Vice Chair of the Education Program and Director of General Surgery at the University of Pennsylvania. And it's co-signed by Dr. Robert Roses, who is Assistant Professor of Surgery, Division of Endocrine and Oncological Surgery

at the University of Pennsylvania. Dated May 29th, 2014 to the Panel:

"To Whom It May Concern: We are writing to offer our perspective on the practice of uterine morcellation during minimally invasive hysterectomy. Drs. Hoonan Noorchashm and Amy Reed were recent trainees at the hospital at the University of Pennsylvania. We became aware of the practice of free intra-abdominal morcellation of uterine tissues when Amy was diagnosed with a uterine leiomyosarcoma. We were deeply saddened to hear of Amy's early peritoneal recurrence, likely a result of morcellation of her tumor during minimally invasive hysterectomy.

"Free intra-abdominal morcellation of specimens is not commonplace in general surgery or surgical oncology. While inadvertent fragmentations of specimens is, in some circumstances, unavoidable, the systematic free fragmentation of tissues within the abdomen during insufflation has no precedent in our fields. The possibility of occult malignancy is always present during operations for benign indications and should influence operative approach. Moreover, alternative techniques for the safe extraction of larger specimens through limited incisions exist. It is therefore our opinion that the purported advantages of uterine morcellation during hysterectomy do not justify the associated risks."

That's the end of the letter. I wrote a letter to the Panel also during the comment period. I'm a Professor of Law at Fordham University in New York City. Now, my area is corporate and securities law, and so I don't

really have anything to add about the medicine. But what I do think I have to add is about the approach, possible solutions to the problem. And I appreciate the desire of regulators to look for moderate solutions to problems and to not appear to be extreme. And one moderate solution that regulators sometimes look to is disclosure or informed consent, especially in my field, securities law. It's a principal way in which regulators regulate.

But what I would like to say to the Panel is that informed consent or disclosure regulation in this context is inadequate. In this context, disclosure protects doctors. It does not protect patients. Informed consent is a legal liability shifting tool. And in this particular context of morcellation, where the risk is undiagnosed or misdiagnosed cancer, you have to ask the question of how will that disclosure work.

There are two people in the room that don't think the patient has cancer when they give the warning. The two people are the doctor and the patient. The doctor doesn't believe that there is cancer present and feels like it's okay to go ahead with morcellation. So the things that the doctor is going to say when the doctor shades the advice to the patient are going to cause the patient to not take the cancer risk as seriously as they should. Second person in the room who doesn't think they have cancer is the patient. So the patient isn't going to hear the cancer risk because the cancer is misdiagnosed or undiagnosed at the time when they're receiving the risk.

Now, legal scholars, my colleague, Omri Ben-Shahar at the

University of Chicago, has a book about the inadequacy of informed consent in a variety of fields. And he focuses on medicine as well. In legal and regulatory scholarship, we've turned away from mandatory disclosure solutions as a solution.

So my own message, as opposed to the message I just read in the letter, my own message to this Panel would be please don't think that you're being moderate by reaching for a disclosure solution. That's an immoderate solution. It's no solution at all.

Thank you.

(Applause.)

DR. DIAMOND: Thank you.

The next speaker is Sara Trainer.

MS. TRAINER: Hello. I want to thank you for the opportunity to speak today. I'm speaking to you today as a teacher, a woman, a daughter, a sister, a mother, and a very concerned citizen. I do not have any financial contributions or connections with anything.

I'm concerned as I sit here yesterday and today and see members of the Panel dozing off, not paying attention and admitting it, when this is a tremendous, tremendous tragedy that is affecting many, many women every year. So, first, that's my first concern.

My second concern is we have spent a significant amount of time yesterday and today speaking about the numbers, 1 in 7,000, 1 in 100, 1

in 500, 1 in 400, 1 in 350, when those numbers really, really do not matter. The more time we spend looking at those numbers and saying, oh, is it 1 in 350, is it 1 in 700, more women are dying, more blood is being spilled, more women are laying on that table with their lives being destroyed, and that blood is on our hands until we do something about it.

This tragedy has been going on for 20-plus years. It was only recently brought to the FDA's attention because of Dr. Reed and Dr. Noorchashm. Twenty years. I'm an educator. I'm a mother. I have no medical background. I rely on people like those of you who are doctors in this Panel to tell me what's right for me because that's your profession. This has been going on for 20 years. It's unacceptable.

We now know, you now know that using a power morcellator upstages cancer, kills women, destroys lives. It's now is the time, right now is the time to make the decision to stop that, and we are calling for a ban on using power morcellators during any kind of cancer surgery, not just uterine, not just in the case of LMS, but in all cancers.

Thank you.

(Applause.)

DR. DIAMOND: Thank you. The next speaker is Steven Goldstein.

DR. GOLDSTEIN: Good morning. My name is Dr. Steven Goldstein, and I am acquainted with some of the members of the Panel, but

not all, so please allow me to introduce myself to those who don't know me. I'm a Professor of Obstetrics and Gynecology at the New York University School of Medicine, a past chairman of the American Congress of Obstetrics and Gynecology, the New York section, and currently President of the American Institute of Ultrasound and Medicine.

My academic and research interests have been mainly in gynecologic ultrasound and evaluation of the endometrium, with special emphasis on abnormal uterine bleeding. I was an invited author for ACOG's *Green Journal*'s expert review series, contributing the modern evaluation of the endometrium.

I've had a clinical practice for over 30 years at this point caring for mainly perimenopausal and menopausal women. I have performed well over 2,000 operative hysteroscopies. I've championed saline infusion sonohysterography for over 20 years, so virtually the only patients I bring to the OR for hysteroscopic surgery have proven uterine abnormalities.

My sympathies obviously go out to anyone who's been harmed and their family with this or any other surgical procedure, and I applaud the Agency and this Panel for undertaking the very difficult task of trying to balance risks and harms.

But the reason I have come here today and at my own expense and with no affiliation whatsoever with any operative equipment manufacturer is that I am extremely concerned that the perception about

laparoscopic power morcellation not in any way be extended to hysteroscopic morcellation devices. I believe it is essential that the Agency make a strong statement to the public and physicians about the differences.

Prior to the hysteroscopic devices, most polyps were visualized but then removed blindly with forceps or curettes, and not infrequently, portions were left behind. The current hysteroscopic morcellator devices allow safe removal under direct vision and are really one of the greatest advances in hysteroscopic surgery over the last two and a half decades.

Previously, intracavitary myomas were resected using a resectoscopic loop and monopolar electric current. Problems with perforation, bowel injury, fluid overload were well recognized and accounted for significant morbidity and, unfortunately, even some deaths. As I'm sure the Agency appreciates, hysteroscopic morcellation because fluid, not gas, as the distending medium allows the tissue to be immediately and completely sucked into the system.

I cannot emphasize enough the value of hysteroscopic diagnosis and removal of intrauterine pathologies allowing accurate diagnoses, which are often curative by themselves, or based on pathologic evaluation allow for appropriate next-step either simple hysterectomy by generalists in some, and rarely, but appropriately, oncologic surgery with staging in others.

Recently, I had a patient referred to me for a perimenopausal

abnormal bleeding who had a history of a previous endometrial ablation. Her cavity was scarred, shrunken, and deformed. I managed to get a small ribbon of saline in on sonohysterography, enough to see a small polyp at the fundus. At hysteroscopy, I could not pass the scope beyond some dense adhesions and attempted to do some curetting blindly, unsuccessfully. Using a hysteroscopic morcellator, I was able to open the cavity safely under direct visualization to sufficiently see the polyp and remove it safely under direct vision. Final pathology was simple hyperplasia, and she is now being treated with progestational agents.

I cannot begin to count the number of times prior to the introduction of the hysteroscopic morcellator that I visualized a polyp seen on sonohysterography, removed it with forceps or curette only to realize on reinspection that pieces were left behind. The ability of the morcellators hysteroscopically to do this under direct vision while avoiding the electric current necessary for the resectoscope has been a tremendous improvement in hysteroscopic surgery.

I am aware of situations where chief medical officers, never gynecologists, responsible for one or more hospitals had ordered all morcellation devices pulled from all ORs after the initial widespread publicity about laparoscopic power morcellation. This is an unfortunate occurrence which I believe was not in patients' best interests.

I am submitting this based on my extensive experience and

three decades of watching the field grow and mature. Any restriction on hysteroscopic removal under direct vision would be a major step backward. I feel that I stand here today representing thousands of clinicians as well as a multitude of patients who need to be protected and need an advocate. As I stated earlier, I have no relationships with any manufacturers of hysteroscopic or surgical devices. I do, as some of you know, have extensive relationships with some pharmaceutical companies as well as ultrasound companies.

DR. DIAMOND: Please wrap up.

DR. GOLDSTEIN: Once again, what I'm asking of the Agency is that in any future notices about morcellation, that the Agency clearly and affirmatively state that this does not apply to hysteroscopy because silence on this has led to confusion among some physicians and patients.

Thank you.

DR. DIAMOND: Okay. Thank you. The next speaker is Bridget Caradori.

MS. DALEY: Good afternoon. My name is Colleen Daley. I am the sister of Patricia Marie Daley, and this is my sister Bridget Caradori. We're here to talk about the morcellation of my sister in 2011. She worked for the Government Accountability in Washington, D.C. Here are some slides of when -- how -- the process.

I want to read to you an excerpt from her operative note.

"Now we are faced with the removal of this huge uterus. We tried first morcellating it. We used two morcellators and then another morcellator. However, the fibroids are so calcified, we were unable to accomplish this. We tried to morcellate the mass vaginally without success. Because it was so big, we could not bring it into the vagina. Therefore, I made a small suprapubic incision large enough to admit another tool and again morcellated the uterus, bringing it out the suprapubic incision."

Her surgeon used four separate morcellators.

In 2011 our sister was postmenopausal when she was told she needed a hysterectomy because her uterus with two presumed fibroids were increasing in size. In three months, they have grown 2 cm. Our sister was petrified of cancer and elected to have a full hysterectomy believing it to be a precautionary measure. Our sister would never have agreed to this procedure if she was told there was a chance of spreading the cancer. She trusted her doctors to do no harm.

In February 2011, she underwent the power morcellation of her uterus. The pathology review came back as benign. It was not until five months later when the slides were reread and the diagnosis of ULMS was confirmed. On July 6th she was rushed from work in excruciating pain. A scan found many tumors throughout her body. She underwent debulking on July 24th where 13 tumors scattered throughout her abdomen were removed. As she waited for her doctors to decide about her treatment, pain

again sent her to the emergency room. Our sister was admitted to the hospital when the tumors returned with a vengeance. On August 31st, 2011, a 23 cm mass was found as well as two tumors on her lungs and smaller masses throughout her body. Our sister left her home on August 30th, 2011 and would never step foot in it again.

What we saw in that hospital was so terrifying, my young niece fled from the room and we burst into tears. There in the hospital bed was a pale and frightened woman. Our sister was lying in there unable to move. Her face was sunken and her eyes were filled with fear and pain. During the coming weeks, as the tumors encroached on her vital organs, she began to experience edema in her legs. Her legs began to swell to the point where they began to leak, leaving puddles. Her incisions on her feet were breaking open. Our sister's once tall and beautiful body became ravaged by the cancer. She would wash her face crying, "Don't look, don't look," as her face and body became skeletal. As my sister took her last breath, our father kissed her saying, "I was here for your first breath; I'm here for your last."

I ask the Panel: Would you permit your wife or mother to undergo a procedure that has 1 in 350 chance of spreading cancer all over her body? So I ask again if doctors cannot be sure if cancer is not present, if there no way to discern this cancer, then would it not make ethical and moral sense to treat all fibroids as if it was cancer and do not morcellate?

I ask for my sister, my family, and all women: End morcellation

of the uterus, and we will believe you will make the right choice.

MS. CARADORI: My daughter could not be here. But in part of helping her cope with the situation and seeing such a rapid change -- she was very close to her aunt:

"My aunt and I were very close. We talked almost every week." And I know they shared corny jokes.

"I always imagined what my life would be with her in it. She would come for my high school graduation. Then I would be living with her and attending college in Maryland or D.C. She would be there for all of the milestones in my life. Instead I'm living in a world where she never got to see me graduate, where I find myself realizing the exact color of her eyes will be lost to me forever.

"The way her voice sounded is slowly fading from my memory. I can no longer recall the beauty of her rare smile. Thank you to the Panel. My sister's dying wish was that no other woman would ever suffer this fate. I know you have great power. You have power to grant a wish. Please end uterine morcellation for all of the women."

Thank you.

(Applause.)

DR. DIAMOND: Thank you.

The next speaker is Sarah Salem-Robinson.

MS. SALEM-ROBINSON: My name is Sarah Salem-Robinson.

I'm a volunteer, scientific advisor for LMS Direct Research Foundation. I'm also a morcellated uterine LMS patient.

Thank you to the Panel members for the opportunity to speak. LMS has offered to pay for my airfare, but I'm not sure I'm going to take it.

Over the last six months, I have compiled over 100 uterine LMS patient histories mirroring my own. And one recurring story stands out. Many recount the same dialogue from their doctor: You don't have cancer. And the, so sorry, it's just bad luck.

We as patients were lethally harmed by morcellation. We are terminal. We cannot reset our clocks nor the hellish emotional damage our families have endured. An oncological faulty device, the morcellator has severed many lives, a device that, one, spreads cancer in a woman's body; two, has erroneously been accepted in the GYN practice for two decades; three, is justified for routine use under the guise of improved, cutting edge technology and better cosmetics. But the stark reality and the bottom line is that the morcellator tool allows cost savings profiting GYNs and their institutions, not the patient. It's ironic that a minimally invasive surgery is maximally invasive.

Presurgically, I requested but was refused an open surgery by my GYN surgeon. My surgeon was certain I did not have cancer and consequently told me, you do not qualify. I was also refused any further scanning. I'm a Stanford-trained PA, a physician assistant, specializing in

OB/GYN and reconstructive plastic surgery, well versed in the operating room, including laparoscopic surgery. I fully understand the consequences when the surgeon pulverizes a mass that cannot be proven definitively negative for malignancy.

How do I -- which one is it? This one?

UNIDENTIFIED SPEAKER: Yes.

MS. SALEM-ROBINSON: Okay. Thank you. I have personally seen the splatter of tissue and spray of cells that is spewed towards the peritoneum cavity during the rotation of the morcellator blades. Just as my GYN surgeon shrugged me off for my concern of malignancy, many GYNs and medical centers still vocally support morcellating fibroids despite FDA's discouraging safety platform. They are gambling with women's lives.

After my diagnosis, my surgeon's reply was, I wouldn't have morcellated you if I knew you had cancer. We with ULMS, uterine leiomyosarcoma, know it is not our GYN's fault that we have cancer. What we refuse to accept is the senseless and unethical risk our surgeons took to allow the spread of our cancer. Nearly all of us diagnosed with Stage I had the possibility of a surgical cure had we had the correct surgery to remove the uterus en bloc or intact.

Our surgeon's catastrophic choice to morcellate us included: one, not informing us that cancer was a rare possibility; two, not letting us know that morcellation could spread a deadly cancer; or three, in my case,

repeatedly and blatantly refusing to allow my request for an open surgery.

Why? I believe it is due to complacency and comfort. I believe these are the blinders worn by the GYN societies, administrators, and the morcellator manufacturers. Or could it be incompetence? Morcellation was recklessly adopted for elective fibroid surgery. All knew the deadly risk, documented by abundant medical journals in the last 10 years. Many GYNs who are surgeons or colleagues on this Panel probably came across a ULMS diagnosis with morcellation.

So why is it that the first adverse event with morcellation was only reported seven months ago? Members are surfacing in our foundation that are patients previously diagnosed with scalp or extremity primary LMS. In reality, they were diagnosed -- they were misdiagnosed and found to have advanced mets originating from uterine LMS morcellation.

This begs the question: How many missed morcellated ULMS diagnoses are erroneously thought to be benign? After all, pathology is challenging for ULMS, and it's often misdiagnosed.

DR. DIAMOND: Please wrap up.

MS. SALEM-ROBINSON: And morcellation or scrambling -- excuse me?

DR. DIAMOND: Please wrap up.

MS. SALEM-ROBINSON: I have eight minutes?

DR. DIAMOND: You have five minutes.

MS. SALEM-ROBINSON: I asked for eight minutes. I'm with LMSdr. Please allow me to continue.

DR. DIAMOND: All right. Go ahead, please.

MS. SALEM-ROBINSON: Thank you. I appreciate it. This is important. And morcellation or scrambling the tissue makes a diagnosis that much easier to miss. I suspect -- you know, I don't know why I was -- okay. In reality, they were misdiagnosed and found to be advanced mets originating from uterine LMS morcellation. This begs the question: How many missed morcellated ULMS diagnoses are erroneously thought to be benign? After all, pathology is challenging. I suspect the risk of hidden uterine sarcoma may be much greater than 1 in 350, but the morcellator's deadly harm doesn't stop there. It extends beyond sarcoma, to include hidden cancers, such as cervical adenocarcinomas, endometrial cancers, BRCA-positive patients undergoing prophylactic hysterectomies.

Morcellation is lethally harmful and avoidable. It is bad medicine, and its mechanics is oncologically faulty. Safer and suitable surgical options exist. Vaginal hysterectomy and mini-laparotomy eliminate all risk of upstaging cancer, or most. I applaud medical centers that have banned the morcellator use. Yet, astoundingly, the two big brother GYN societies, the three big brother, ACOG, who we've seen, AAGL, and SGS, refuse to restructure their policies on morcellation, all under the pretense that the benefits, basically cosmetically pleasing surgery and a quicker return

to activities, for the majority of women outweighs the deadly risk for the few.

Is this ethical thinking, to allow deadly harm to a patient? What benefits are the GYNs haggling over? Could it be the morcellator eliminates the need for two hospital stays, allowing more profits for both medical insurers and institutions? Why is it that GYNs assume a mass is benign versus other specialties that consider a mass to be malignant until proven benign? In addition, what are the complications that are unique to morcellation that don't cause cancer upstaging? And how many women will need to suffer through parasitic benign uterine implants that cause chronic pain, infection, and obstruction that may need an emergency surgery? Is the oncological faulty morcellator worth it in GYN surgery?

Taking a supportive stance to the FDA's statement, Johnson & Johnson, the largest manufacturer, announced a moratorium pending today's hearing results. My first response was to applaud their action. Yet, recent media disclosure of their faux pas makes us question their underlying motives. Publicized last month, a revealing dialogue ensued between pathologist Dr. Lamparter and Ethicon eight years ago, in 2006, who dismissed repeated warnings that were nearly identical to the FDA's safety advisory.

Long overdue, GYN societies must reconfigure their policies for the good of women's health. All parties must accept accountability. They must change their comfortable and highly lucrative morcellation practice and

return to the medical oath, first and foremost, do no harm. Additionally, the FDA needs to regulate safety by revamping the 510(k) licensing on medical devices that will ensure prevention of a future device atrocity.

Requiring a log of a medical device adverse events and complications with periodic reviews for routine devices is imperative. It's not enough that the GYN societies would like to agree that a woman sign a transparent informed consent of risks, releasing them of liability, nor is it enough that a bag be used during morcellation. Bags can be defective or break. In addition, for the surgery, bags can be very difficult to work with and can obstruct the visual field, resulting in major deadly complications like severing main veins or arteries.

DR. DIAMOND: Please wrap up now.

MS. SALEM-ROBINSON: Yes. Thank you.

Breaks can occur allowing permeability of cells. Side with the patient, not the device. If you can plan to have a larger incision, then why not do a mini-lap that would spare any risk of spill? We talked about bringing the bag out through -- to -- an extra 2 to 3 cm incision.

Again, I cannot stress enough there's alternative safer surgeries, and I implore the FDA to step up and dutifully protect all women who are mothers, daughters --

DR. DIAMOND: Thank you for your presentation today.

(Applause.)

DR. DIAMOND: The next speaker is Hector Chapa. Okay. Not seeing Dr. Chapa. Next speaker is Alison Perate.

DR. PERATE: Hello. It's my pleasure to be here and speak on behalf of those who cannot speak for themselves. I'll give you my credentials just to give you a background. My name is Dr. Alison Perate, and I am fortunate to be practicing at one of the top institutions in the country. This is important because there is a lot of misconception being thrown around this room. I trained at the University of Pennsylvania. I did my fellowship at the Children's Hospital of Philadelphia, number one in the nation, and I held a double appointment in both University of Pennsylvania and Children's Hospital as a practicing physician scientist. As a board certified anesthesiologist, I live in the OR. I watch this every day. Not morcellation, but surgery, so I know what I'm talking about.

I came straight here from work yesterday. I actually didn't even have time to change. I was in bloody scrubs and my white coat, which I had intended to wear here, but I couldn't bring myself to do it. For the first time, I was ashamed as a physician. I'm ashamed to wear that coat. I cannot believe that we are here today with colleagues that have studied medicine and are defending this practice, knowingly putting patients at risks and knowingly killing them.

This is against everything I trained for. This is against everything I spent the better half of my life working 100-plus-hour weeks for.

I spent the better portion of my life training, and when I graduated from medical school, the dean said something so important that I wish to pass it on to you. He said do not forget the words behind your name are M.D., not G.O.D. Never forget this. You are here to help, to heal, to cure.

That is our calling. We do not make these decisions lightly, and we sure as hell don't have the ability to make decisions of life or death for our patients. We take an oath, the Hippocratic Oath. The fundamental principle of that is primum non nocere: First, do no harm. For those of you that are unfamiliar with this principle, it means that the well-being of the patient is paramount, not their convenience, not how soon they get back to work, not their satisfaction with their surgical scar. No. It is their well-being. Were these patients' well-being being preserved when you did these morcellations? I ask you that. No, they were not. They did a lot more than harm. They killed these patients.

I have taken part in countless surgeries. We are one of the top laparoscopic institutions in the nation. When I got the diagnosis from my brother-in-law Hoonan that my sister Amy had a uterine sarcoma, I asked him the very simple question: Clear margins, right? They got it en bloc? That was the first time I heard she was morcellated. I ran immediately into our laparoscopic surgeon's OR and said: What is this? We morcellate unknown pathology in free abdominal cavities? And he looked at me and said absolutely not. And I said, oh, well, it was done, and it was done to my sister.

He was appalled. He is top in the nation in laparoscopic surgery. So I asked him: How is it possible that I've never seen a morcellator used in one of our ORs? I do this every day. His answer: Over a decade ago, Ethicon, a J&J subsidiary, had brought their morcellators to be tested, and we have a simulation lab. Before we stick them in humans, we try them in our sim lab. The same company that Dr. Isaacson receives royalties from, Ethicon, this company brought their toys in. Our surgeons attempted to use them and found them to be "too dangerous to place inside of human beings." The uncontrolled spillage of unknown pathology was not acceptable to them. They were, at that time, a decade ago, placed and permanently stored on the shelves of our simulation lab, never to have been brought into our operating rooms.

Again, I tell you thousands of laparoscopic surgeries a year, I personally take part in many of them, we have never once used a morcellator. So do not equate morcellation with laparoscopic surgery.

Okay. So let's start talking about this. Let's see where we're going, because although Dr. Jubilee Brown wants to talk about a balanced approach, I think she missed the second half of that balance. So let's go there. So this is the problem of detachment. I asked you, these OB/GYNs, if these women that they were operating on died immediately there on the OR table, 1 in 300, 1 in 500, 1 in 1,000, 1 in 7,000, would you take that risk? Because, personally, I remember the face and the name of every patient that

has ever died on my operating room table. I remember the circumstances, and I have wracked my brains for months, weeks, years trying to determine what I could have done differently to maybe make their lives different. No. What if the gynecologist exploded on every 1 out of 350 or every 500, would you still find that an acceptable risk, to stick that in the patient? No. This is Russian roulette. You're basically sticking a loaded barrel into these women's abdomens, spinning the barrel, and hope that the bullet doesn't come up. This only occurs because these women go off to die quietly, painfully agonizing deaths in hospice with their family around.

Let's talk stats, because I only have a little bit of time left. Basically I can bring up any study you want. There's no difference except for hospital stays. Maybe a little bit extra cost in laparoscopics. Complications, same; death rate, same. And *n* of fives that some people are talking about in their studies, here's a study of 10,000 hysterectomies: blood clots, same, no statistical difference; death, no statistical difference. The only thing that mattered in any of these studies was experience level of the surgeon, not the approach.

So for you to sit here and pretend like this is about saving women from abdominal hysterectomies -- 10,000 patients, how many more numbers do you need to see? There is no difference. You're not saving the women from anything except a couple of days in the hospital. And I ask you, ask Amy Reed, my sister; ask Al, his wife, Sally; the Jacobson sisters, their

sisters, how many days in the hospital are worth those lives? That's what you need to ask yourselves.

I hope you have the wisdom of Solomon here to see that we should not even be discussing this. This should not even be an issue. It's our responsibility as a field, it's our responsibility as physicians to take care of our patients and to live up to that level of trust that they instill in us to do that.

Thank you.

(Applause.)

DR. DIAMOND: The next speaker is Lisa Nielson.

MS. NIELSON: Hi, my name is Lisa Nielson, and I have no affiliation or interest with anyone but women.

In 2009 I had a hysterectomy. My uterus and fibroids were morcellated. I went home, and I recovered, and I had my follow-up appointment, and I was told everything was fine. And I was doing well. I had five small scars on my stomach, and I was up and about in about a week. And I went on with my active life, a mother of three girls and a wife to my husband, and my daughter, the only daughter to my parents, their only child.

And then about a year and a half later in May, I started having problems. I started feeling pressure on my bladder. And so I made an appointment with the specialist. And then that was a specialist, so it was taking about three weeks to get in. I started feeling a bump down in the pelvic area. And I decided I would go in and see our family doctor. And that

prior February, I had had an appointment with the gynecologist that I had been seeing for my fibroids, not the surgeon, because she recommended me out to a surgeon, but for my regular gynecological examination. And she did a very thorough examination and nothing was there. So now we're in May, and there's a bump, and I go see my primary doctor. And she's very alarmed, and she says I don't think -- this isn't your bladder. I want an ultrasound immediately. And so she ordered one I think the next day, and that came back with showing that there were growths.

And so she immediately wanted a PET scan, and so we immediately did a PET scan, and things are getting alarming. And then they did a core biopsy, and things are getting alarming. And at that point, we're realizing that there's cancer. And I am referred to a gynecological oncologist surgeon. Then I go see him. And I sit in the room with my mother and my husband, and he looks at everything, and he tells me that I have uterine leiomyosarcoma, and it's most likely Stage IV.

Wow. My world shattered. It was devastating. My husband and my mother and I were stricken. We came out and met my father. I texted my best friend. It was hideous. Things happened quite rapidly then. We started our research. We realized what Stage IV uterine leiomyosarcoma meant. We were horrified to figure out that the morcellation had seeded it. The doctors made it very clear that it had seeded it. So the fight began. The fight. That's what I want you to understand is what this does to women. It's

not a quick and painful death on the operating table, which I know you would be alarmed at, as Alison pointed out. It is a fight like no other fight, and that's what we're asking you to protect women from. That's what we're asking you to do something so drastic about is to ban morcellation, to tell the technology companies to go back to the drawing board. It's because of the death and destruction.

This is a picture of me with a 25-pound tumor, one of seven. I hope you read my letter, my mother's letter, and my daughter's letter to understand the impact that this has. So there you can see the four of the scars from the laparoscopic. This tumor grew fast, super-fast. I just felt it when it was in May, and this picture is taken in September. We tried two different types of chemotherapy. It kept growing. I ended up nutripedic in the hospital for five days needing several blood transfusions and plasma. And then, finally, in September, I had an eight-hour surgery to remove this 25-pound tumor, which looked like this. It was 37 cm. And the six others that were by my spleen.

Minimally invasive, minimally invasive, right? That's what minimally invasive ended up looking like. That's 85 staples. I was in the hospital for seven days over the summer; it was 21 days. My recovery took over five weeks. At points, I thought I wouldn't make it through the recovery. I weighed 109 pounds when I left the hospital. I had no hair from the chemotherapy. I was depleted.

I stand here before you asking you, for women, to do this, to protect us, because we can't protect ourselves. We listen, and we believe our doctors. So if they tell us they believe it's safe, based off of statistics, we believe them. And then we get a phone call, and we're told we have Stage IV cancer. It's not acceptable.

At one point in time, I would have blamed this on the morcellation companies for not doing their due diligence. But after today, the responsibility lies with you, with each and every one of you. It lies with you. We will do our part through social media, through Facebook and Twitter and through the media to spread the word. And what you do will be scrutinized through those networks. But I'm going to trust in you as I pray at night for you to do the right thing, to ban this, to tell them to go back to the drawing board to come up with something safer, completely safe.

I thank you so much for doing what you do. I appreciate it so much. Thank you.

DR. DIAMOND: Thank you.

(Applause.)

DR. DIAMOND: The next speaker is Debra Valverde.

MS. VALVERDE: Good morning. Respecting hearing protocol, I have no financial affiliation.

My name is Debra Valverde. I am a mother, grandmother, wife, sister, daughter, educator, and a victim of Stage IV leiomyosarcoma

caused by an outpatient laparoscopic hysterectomy procedure done in 2007 by morcellation. In May of 2011, I was shocked when I learned the news that I had LMS. It began with a visit to my primary care physician just to look at a bump on my scalp that seemed to be growing. I remember asking her if it was cancer and her reassuring me that it was only a cyst, that she saw it all the time.

A few months later, I would return to have the cyst drained only to hear the dreaded words, "I'm sorry, Ms. Valverde, you have cancer." I was devastated. I was misdiagnosed. A year later, in June 2012, the cancer metastasized to my sacrum, upgrading the leiomyosarcoma to Stage IV. In February of this year, just a few months ago, I would again be misdiagnosed, this time with sciatica. After three weeks of excruciating pain, I would eventually learn that the cancer returned and the growth of the tumor was crushing my spine resulting in severe nerve damage and more cancer infused in my bone.

It is my hope that by sharing my story, I can also educate you as to what can occur when the procedure of morcellation is used during a laparoscopic hysterectomy. This procedure has turned my life upside down. It has crushed my dreams. It has devastated my husband, children, and my entire family. I cry every single day. Who will love my children? Who will take care of my 82-year-old father, who was just diagnosed with dementia, because I'm his caregiver? How do I say goodbye to all my family and friends

that I love so much?

I am helpless and I am angry. I am angry because I was never given a choice. Moreover, I am angry because I was never informed that having laparoscopic surgery by morcellation would end my life. I am waiting to die. I am counting the days. I beg you, I beg you please stop morcellation.

Thank you.

(Applause.)

DR. DIAMOND: Thank you. Thank you.

The next speaker is James Leary, Jr.

MR. LEARY: Good morning. Over the past day and a half, I have been sitting here. I've heard this Panel. I've heard industry experts. I've heard other medical experts talk about numbers. I'm going to talk about one number. That's my wife, Barbara, which you saw on the poster center where she lost her battle with cancer in September of 2013.

I'd like to give you a little background about myself. I have no financial assistance. I paid for this entire trip by myself.

My wife and I were considered the odd couple. We lived in upstate New York. We were an average family. Two daughters in a local high school. My wife worked for the Diocese of Rochester as a daycare provider and the director of a daycare. I worked for a local municipality, been a police officer for over 28 years.

The reason I say we were the odd couple is even when we

started dating, through our courtship, and even through our marriage, my wife was always health conscious. She would run constantly. She would run 5K races. She would exercise on a daily basis. What do you think I was? I was the opposite. I ran to the refrigerator. I ran to the pantry. I slept horrible hours working all types of shifts, getting called in at all hours in the morning, days, holidays, and everything else. I ate junk food. I ate fast food. And she used to say, this is going to kill you, this is going to kill you. And unfortunately, I am here, and she is not.

In March of 2009, my life, my family's life changed forever. Her OB/GYN of over 16 years who had been monitoring her for fibroids suggested that she have her fibroids removed. On that day, she went to Rochester General Hospital. I have original documents and copies here that if anybody wants, you can get a hold of the liaison. I'll be happy to meet you anytime and anywhere to show you. I will not disseminate them here for them to go wherever.

I think it's important, and I'll show you the stationery here, to read a couple of the attachments here. And it goes through the robotic-assisted surgery and says that the camera's attached to one of the surgical system's robotic arms. The other two or three arms hold the instrument such as a dissector, scissors, scalpels, and forceps. These instruments were able to grasp, cut, dissect, and suture structures inside of the abdomen. It goes down to say how the surgeon uses hand controls, et cetera, et cetera.

At the bottom it goes: "In the process in which organs or tissues are removed, the specimen is placed into a bag or is cut smaller to be removed through one of the incisions in the abdomen. Once this procedure is completed, the instruments are removed and the surgeon closes the incision." On the back, it happens to go through the pros and cons, which we've already heard, so I won't go over it again. And in the end, it says, "Two of our partners," the two surgeons that performed the surgery on my wife, "are now performing these advanced surgical procedures for our patients at our location. We are so pleased to be able to provide this type of surgery as an option to our patients."

When we went for a consultation, my wife had three fibroids, and one was growing, which concerned her OB/GYN. And obviously my first question was, well, is it cancerous? I was told fibroids are 99.9% noncancerous. Don't worry about it. This is a safe procedure. I knew nothing about power morcellation.

When a reporter from the *Wall Street Journal* contacted me several months ago after my wife's passing and wanted me to provide her history, I got the report from the hospital. And in here, it says that she had an extremely large fibroid uterus. If you want to see it, this is not my writing. This is the doctor's writing. "The patient had a 20-week fibroid uterus. The cervix appeared normal. The anatomy of the bladder appeared normal. Normal appearing of the liver's edge, normal appearing of the appendix," so

on and so forth. Her assistant -- you want to talk about numbers. This says a 20-week fibroid. The assistant who was with her in the operating room, he said 24-week fibroid. So two people looking at the same can't even come up with the same number, and you're worried about numbers?

My question to you, respectfully submitted, is that we were never told of anything of morcellation. Morcellation was never ever used in any consultation, preop, postop, or anything. But when I get the surgical report, page 2, "At the point a 15 mm morcellator was placed into the left accessory port, the fibroid and uterus was morcellated and removed." Down at the bottom, it says, "Specimens to pathology of the uterus were in multiple sections."

So my question is that listening to these experts and these medical experts and so on and so forth, why don't we get a nice little 3 by 5 index card or trifold saying, I'm the manufacturer of this great power morcellator. We're number one in the country. We do all these surgeries. In my work as a police officer, when people leave things out, there's a reason. The reason is they're hiding something. And I implore all of you to make them come forward with their information, because they know the real results.

And I want to thank the FDA for their presentation yesterday. In the short time that you had to put that together, I think it was well put together, it was informative, and I thank you for everything.

Thank you.

(Applause.)

DR. DIAMOND: Thank you.

The next speaker is Negin Griffith.

DR. GRIFFITH: Good morning. Have to lower this a little bit. Good morning. My name is Negin Griffith. I am a board certified plastic surgeon, having also trained in general surgery. I sit on the board of my professional organization. I write the questions for the in-service exam that our residents take every year. I'm also on the board of my hospital foundation and on the medical executive committee. I'm also the sister-in-law of Dr. Amy Reed and sister to Dr. Hoonan Noorchashm.

You know, I wasn't planning on speaking today. I almost, despite the catastrophe that this has been for our family, I tried to enter the room yesterday putting myself in your shoes, as an objective individual trying to make a decision on this very important issue. But I have to say after listening to yesterday's testimony, I felt compelled to say a few words today, and I appreciate you giving me the time to do so.

What I heard yesterday was a lot of data about the benefits of laparoscopic hysterectomy as a defense of the technique of morcellation, as if the two are synonymous; you can't have laparoscopy without morcellation. That's not true. We see colon cancers resected laparoscopically with all the benefits that laparoscopy has to offer. Kidney cancers are removed

laparoscopically. We harvest kidneys for transplantation laparoscopically, all without the use of a morcellator.

In fact, I've seen my own gynecologic colleagues do a laparoscopic dissection of a uterus, place the specimen correctly in a bag, and remove it through the vagina. In a very rare case in my training at Magee-Women's Hospital, I've also seen the occasional gynecologic surgeon do a laparoscopic or robotic dissection of a uterus and remove it through a hand port, as we do in colon cancers. So it can be possible. Those two techniques leave behind really a very small percentage of women who will then have to have open abdominal hysterectomies. Laparoscopic surgery can be done without the use of a morcellator.

When Amy was first diagnosed, my brother called me, clearly upset, understandably so. And he said that her pathology revealed leiomyosarcoma. We both knew what that meant. I comforted him saying, okay, thank goodness she had a hysterectomy. It's out.

Now, this was a conversation between a surgeon, who has done general surgical training and plastic surgical training, another surgeon who's completed a general surgery training and a cardiothoracic fellowship, talking about an anesthesiologist. None of us were prepared for what we heard next, that Amy's tumor had been ground up in her abdominal cavity and her cancer upstaged due to the technique of morcellation in order to save her one or two hospital days, in order to save her a few extra days on

the couch, in order to save her 45 cc's of blood loss, in order to save her a treatable incisional infection.

You see, as a general surgery trainee, we are taught to assume the worst, to never disrupt a tumor no matter the likelihood or unlikelihood of malignancy. You always give your patient the best chance for appropriate treatment, the best chance for a cure.

Yesterday, I also heard people question whether disease is actually spread by morcellation. The tissue is cut from its blood supply, right? So it's going to die. What does it matter? Who cares if a little piece falls off? As a plastic surgeon, my entire specialty is built on transferring tissue that has been amputated from its blood supply to correct something that disease or trauma has taken away. I often take a piece of skin from the thigh. And sure, if you take that piece of skin and throw it in the garbage, it dies. It doesn't survive. You're right. It doesn't have a blood supply. But if you put it in a well-perfused site, not only does it survive, it thrives. The same is true of uterine tumors. The same is true of benign uterine tissue, frankly.

I think the conversation that we're having this week is critically important. I know that no surgeon, no doctor wants to harm their patients. I believe that to be true about my gynecologic colleagues. I know that to be true. Many of them are my dear friends. There are still a lot of questions to be answered about morcellation, but it mustn't be at the expense of 1 in 350 or 1 in 1,000 or 1 in 7,500. It doesn't matter -- higher in the African-American

population. It doesn't matter what that statistic is. It mustn't be at the expense of those lives, because remember, we're not exchanging lives to save 349 or 999 lives. We're exchanging a life to save 349 hospital days, 999 hospital days, or a 10 to 15% of a treatable infection.

We have to take morcellators back to the bench side, prove it to be safe in animal models, and then bring it back to the bedside. Not the other way around. We have to first prove that morcellation does not cause harm before returning it to the market. Not let's wait and see how many people die from this and then decide to do something about it. We must get better at diagnosis, then bring back morcellation. For now, until we can better diagnosticate, we must not morcellate.

Thank you very much for your time.

(Applause.)

DR. DIAMOND: Thank you. That was the last of our scheduled speakers. Do any members of the Panel have any brief, clarifying questions of any of the speakers that we've heard from?

(No response.)

DR. DIAMOND: Okay. Not seeing any, then I now pronounce the Open Public Hearing to be officially closed, and we will not take any additional speakers.

We're going to take a 10-minute break at this point and then resume.

(Whereupon, at 11:43 a.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(1:00 p.m.)

DR. DIAMOND: All right. We're going to go ahead and reconvene the meeting. At this time, we're going to focus on the discussion questions from the FDA. Panel members, I ask that each of you identify yourself at the time that you are speaking in order to facilitate transcription. I'd also like to remind members of the Panel that this is a general issue meeting, and references to specific products and firms should not be included in this discussion. I would also like to remind the public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific request of the Panel Chair.

I'd now like to ask Julie [sic] Blyskun to read the first question you'd like the Panel to consider.

DR. BLYSKUN: Thank you, Dr. Diamond. This is Elaine Blyskun. So we have modified the questions slightly due to the time limitation. We're going to be starting with Question 2. And the question for the Panel is to: Please discuss whether there are any patient or fibroid characteristics, physical exam findings, laboratory and/or imaging tests, or combination thereof, which could assist in determining the presence of an unsuspected sarcoma in a woman with presumed uterine fibroids. If so, please elaborate on what those are and the level of evidence which supports your conclusions

and recommendations.

DR. DIAMOND: Okay. Is there a member of the Panel that would like to address this?

Dr. Brown?

DR. CAROL BROWN: So we do know some things about the epidemiology of leiomyosarcoma. One thing is that we know that it tends to occur in older women. We've heard here, and it's been known for a while, that probably MRI is an imaging modality that can be helpful, and I think it's important to note, not in diagnosing a uterine leiomyosarcoma, but in diagnosing a benign fibroid. I think we heard the data presented yesterday that there's a very high negative predictive value if a fibroid is -- if it's completely circular, low density, homogeneous, et cetera, no abnormal blood vessels. So I do think that, you know, the strict answer to this question, yes, there are some modalities, I think, patient age and imaging.

Also, you know, symptoms and exam findings can be used, I think, to kind of have more certainty that you're dealing with a fibroid. I don't know that we can say we have any modality that can tell you it's leiomyosarcoma other than a biopsy, and we did hear there is some data that endometrial biopsy can diagnose a certain number of leiomyosarcomas. But I think that we do have imaging and things that can help reassure us that someone does have a fibroid.

So I guess that would be -- and I think the level of evidence is,

for MRI, diagnosing fibroids or confirming your suspicion that something is a benign fibroid, is very good.

DR. DIAMOND: Dr. Iglesia?

DR. IGLESIA: Cheryl Iglesia. Yes. I have reviewed all the position statements from the several of the medical societies that have developed them, including AAGL, SGO, ACOG, and they have been listed. They're on our public record. And not only do they include history of genetic susceptibility, you know, when you're doing -- when you have a known genetic reason like hereditary leiomyomatosis and retinoblastoma, or someone who is a BRCA carrier, and you're doing a risk-reducing surgery.

I also think that a lot of the cases that we heard, I question the indication for doing the morcellation in the first place because of the clinical presentation. And I think that there may have been some errors not just by the morcellator but in surgical judgment and patient selection, and an inappropriate use of the morcellator in patients who are inadequately worked up for abnormal postmenopausal bleeding and, you know, may have other risk factors that -- or characteristics that may increase. So I think that inappropriate evaluation or incomplete evaluation for postmenopausal bleeding is a contraindication to the use of power morcellator. And I also understand that previous pelvic irradiation and history of tamoxifen use and very, very careful in older patients with the fibroids, particularly those that are growing.

DR. DIAMOND: Additions from other members of the Panel? Dr. Mattrey?

DR. MATTREY: Yeah, Bob Mattrey. I'd just like to refine a little bit more of the MR side. I think when a fibroid looks benign, meaning dark, well circumscribed on T2, it is benign. But the majority of the difficulty comes when fibroids don't look that way. It's not that we can't diagnose leiomyosarcoma. It's just there is a good percent of fibroids that could look like leiomyosarcoma, and to distinguish those two would be difficult. But if the fibroid is dark on T2, has very little water signal within it or the degeneration is obvious, that's a benign with a very high negative predictive value.

DR. DIAMOND: Dr. Hillard?

DR. HILLARD: Paula Hillard. So I think that this is important for us to understand and important for the public to understand as well, the issues about imaging, because I'm concerned that part of the message may be that leiomyosarcoma or other sarcomas are a common conditions, and the 80% of women that I see who have a small, benign, asymptomatic fibroid are going to be anxious about that possibility of a cancer. And if 80% of all women had an MRI done, I don't think that would be an appropriate conclusion.

So I think that we need to hear the statistics and information but also use clinical judgment in thinking about symptoms and who is at risk.

DR. DIAMOND: Dr. Snyder?

DR. SNYDER: Yeah. Dr. Snyder. I'm not aware of any data to specifically identify an increased risk because of a solitary or dominant myoma, but if you look through, you know, these papers that have been given to us, you know, that is another characteristic that, you know, brings, you know, significantly more concern.

DR. DIAMOND: Dr. Shriver?

DR. SHRIVER: Craig Shriver. Again, as a member of this Panel, I speak only on behalf of myself and not as a representative of the Department of the Army, Department of Defense. And I think out of fairness and respect to the Panel, I just want to sort of let you know where I'm at right now. As I mentioned yesterday afternoon during the discussion, as a surgical oncologist trained in the core basic Halstedian principles of cancer surgery, I'm always myself asking and adhering to and teaching others to adhere to the tenet of treating all masses as cancer until proven otherwise, which is borne out of the ancient Hippocratic principle of patient care and primum non nocere, and first, do no harm.

Having been perplexed over the last two decades, watching the introduction of a laparoscopic power morcellation that is totally anathema to these and my core principles as a cancer surgeon, after these two days of testimony and data, based on science, I have only more strongly reaffirmed my commitment and belief that there is, at present, no safe way to offer

laparoscopic power morcellation as part of any minimally invasive surgery. I conclude and state as a member of this Advisory Committee to the FDA that my position is that the device under consideration, the power morcellator, should have its Class II device status immediately withdrawn and its use in any laparoscopic surgery banned.

Going forward, I answer the FDA questions to the Panel only in the context of what a future submission to the FDA for any new technology related to this approach under a submission as a Class III device with relevant preclinical testing and in the context of properly constituted and informed patient clinical trials prior to any future approach in this field.

I will now answer the FDA questions as requested. So for Question No. 2, there are no tests that I have been shown on the data or the science that either in isolation or together are good enough at this time or in the near-term future that determine the presences of an unsuspected sarcoma in a woman with presumed uterine fibroids. Even in the best studies, the level of evidence of that uncontrolled -- of those data is uncontrolled longitudinal studies, which are low-level evidence.

Thank you.

DR. DIAMOND: Dr. Yustein?

DR. YUSTEIN: Dr. Diamond, can Dr. Snyder clarify what he was referring to when he was talking about the papers and saying that that was a significant concern?

DR. SNYDER: Dr. Snyder again. Again, it's the difference between multiple myomas and a solitary, you know, myoma.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: So I just wanted to add a bit of clarification. I'm also a gynecologic oncologist, surgical oncologist, specializing in the treatment of women's cancers. And I just want to point out that I absolutely agree with the oncologic principles. However, we're dealing with a known benign tumor that affects hundreds of thousands of women in the United States. It's been estimated that maybe one out of every four African-American women have fibroids. And if we follow Halstedian principles, then the logical conclusion would be every woman who has fibroids, whether they're symptomatic or not, because there is as much of a 2, 3, 5% chance that that is a sarcoma, should have her uterus removed. So I think we have to keep that in mind.

Unfortunately, because fibroids are so common, I don't think that we can apply the oncologic Halstedian principles about an abnormal growth that we would like to because the result would be hundreds of thousands of women having an unnecessary operation. So I just wanted to clarify that for the public and for everyone else, because fibroids are a different histologic, pathologic process. We've heard multiple testimony, and it is definitely clear they do not have to be removed unless there are certain problems that they can be causing, which can include severe bleeding,

discomfort, et cetera, but that if we feel that we have to -- only way we can be sure that a woman doesn't have a sarcoma if she has a fibroid is to take out her uterus, you can't ignore that that would result in, again, hundreds of thousands of operations that are not justified.

DR. DIAMOND: Dr. Talamini?

DR. TALAMINI: Mark Talamini. With respect to Question 2, I believe that there are characteristics which can assist in determining the presence of an unsuspected sarcoma in a woman with presumed uterine fibroids, which is the exact wording of the question. And I think those are going to consist of MRI, radiologic evidence, the patient's clinical situation, whether they are post or premenopausal, their age, their race, and other considerations that we've heard.

Since I believe that is the case, I would proffer that somebody do the work, whether it's the FDA or not, to put forward a potential clinical pathway, including those pieces of evidence, that could then be tested against current datasets to determine how much a clinical pathway could be used to reduce the risk of an unsuspected sarcoma being removed in an inappropriate way. And I think there are multiple societies or other professional organizations or academic centers that could contribute to putting such a pathway together with the FDA's concurrence.

DR. DIAMOND: Okay. Other members of the Panel?

Dr. Snyder again?

DR. SNYDER: Yeah, Dr. Snyder again. And, again, the question is stated -- it doesn't say, you know, indications for surgery, for type of surgery or anything. It just says with presumed uterine fibroids. And you know, we heard evidence that growth rate is not consistent between benign and/or sarcomatous, you know, lesions. But that is a characteristic that differentiates somebody from in a higher risk. And, again, it's going to be that kind of data that, you know, will tell us is there a growth rate, you know, that, you know, would be a risk factor.

DR. DIAMOND: Dr. Isaacson?

DR. ISAACSON: I think there's, unfortunately, there's a tremendous amount of gray zone, but I think there are some parts that are black and white, at least in my own mind. And the black and white part has been touched upon a little bit. But one is any, I would venture to say, perimenopausal, postmenopausal woman who has an enlarging fibroid, a fibroid that has recently become symptomatic, a fibroid that's causing abnormal uterine bleeding is not one who should have -- we can discuss whether it should even be a myomectomy, but certainly shouldn't have morcellation.

And just as Dr. Shriver has made some preemptive comments, I want to make a preemptive comment because I'm having a hard time seeing any data that shows a difference between any type of morcellation versus power morcellation. So I'm putting them all together, because I haven't

heard any evidence that says morcellating with a scalpel versus a power morcellator is really any different. They're both -- the issue is still spillage of tissue.

So, again, that part, we could -- I feel very comfortable saying that there is no role for morcellation in a postmenopausal woman with any type of fibroid, new fibroid symptoms. So that kind of addresses a little bit of this question.

The MRI is going to be difficult because, as we've said, if you have a degenerative fibroid -- and I don't know what percentage of the fibroids, maybe the radiologist could tell us, really are clearly dark and well circumcised versus those that you really can't differentiate. I just don't know what that percentage is, and I don't think I heard it yesterday from Dr. Ascher. So I do think it's another piece of the puzzle that should be ordered. And that's what this whole thing is. It's putting together a puzzle to get all the information you can to make the best decision. So I think the MRI is useful. I think the patient's history is useful. I think the patient's age is useful. And that's how I would leave it at this point.

DR. DIAMOND: Okay. Dr. Afifi?

DR. AFIFI: From a statistical point of view, the methods used to develop an algorithm for diagnosis can either be multivariate types, sort of logistic progression, or something. But from everything that I have learned so far, reading the material before coming here and hearing the various

opinions, it seems that a non-parametric approach would be more appropriate, sort of a branching process type of algorithm. For example, if all smooth, round type images are benign, then that would be one branch; if it is not, you go the other way, and so on and so forth. There's a technique called classification and regression trees, CART, that would be very appropriate for that. It would not only identify the optimal way of doing such a tree, but also, it would help with the estimation of the probabilities of wrong classifications going either way. So that's one thing I would propose that the FDA would think about.

DR. DIAMOND: Dr. Wentzensen?

DR. WENTZENSEN: Yeah, Nicolas Wentzensen. I wanted to comment on the use of risk factors, epidemiologic risk factors to assess the risk of leiomyosarcoma. My colleagues and I conducted a large study of combining leiomyosarcoma from 15 large population-based studies, and although we found some risk factors associated with leiomyosarcomas compared to controls, the magnitude of those is not really going to be clinically useful for really assigning risk categories. So I think that's -- I'm skeptical about that. And I think MRI, although we've seen some indication, I don't think we have any specific data to the specific question that we are addressing here, so --

DR. DIAMOND: Okay. So I guess my general consensus of what I've heard from around the table, in response specifically to the question that

FDA is asking, is that there are some indicators that may be able to help us identify the presence of an unsuspected sarcoma, and those are related to MRI imaging, clinical characteristics, including an individual's age and changing clinical characteristics after the time of menopause, a unique subset of individuals with familial leiomyomatosis, also perhaps race, but it doesn't sound like anybody has a great deal of confidence that those are going to be able to accurately predict the vast majority of leiomyosarcoma, and there would be a large number of presumed fibroids that would be in a status where it couldn't be for sure.

Is that a reasonable conclusion of what everyone is thinking?

Dr. Yustein? Dr. --

DR. YUSTEIN: Dr. Diamond, just quickly, I didn't hear anybody mention anything like biopsies or tests such as that, so could I assume that nobody thought that any of those would be useful?

DR. DIAMOND: I think one person did mention biopsy, and it's something perhaps to consider, but I don't know that we have a great deal --

DR. CAROL BROWN: When I said I think that a person needs to -- a woman needs to be appropriately worked up, the workup would include cervical cytology, endometrial biopsy, other imaging that would be indicated like sonohysterogram with directed biopsies, if necessary.

DR. YUSTEIN: I thought you meant that was for women with abnormal bleeding specifically?

DR. CAROL BROWN: Or symptomatic fibroids.

DR. DIAMOND: So were you thinking of uterine fibroid biopsy, or is that what you were asking? Okay.

Dr. Brown?

DR. CAROL BROWN: So as a gynecological oncologist, again, we would not encourage, number one -- it was brought up yesterday -- so you see the size of a fibroid, so the chances that you are going to, if there is some malignant transformation or atypia, or if it's a STUMP, that you're going to be able to make that diagnosis on a needle biopsy is really nonexistent, and it is not worth sticking a needle into something that you could hit the uterine artery, you could hit bowel, you could also spread the cancer.

But it was referred to, I think, in Dr. Brown's presentation -- and I think, actually, a lot of this is us reminding clinicians of what are the established accepted standards of care for workup and evaluation of a patient who is having a non-completely extraoperative procedure; i.e., if you're not going to do hysterectomy for a fibroid, it is standard and accepted practice that we as oncologists try to teach that you must exclude malignancy to the best of your ability. And so if you are not taking that uterus out, you need to do everything you can to exclude the presence of any type of malignancy, not just uterine leiomyosarcoma, but cervical malignancy, endometrial malignancy, and ovarian malignancy and tubal malignancy. You must do that.

And, you know, again, one of the reasons I had inquired about getting more information, and I did get more information by listening to the many people who got up this morning to talk about their stories, is that I think, as Dr. Iglesia referred to, there are probably a lot of situations or some of these situations where common principles, basic principles of how you work up a woman who you're going to do a myomectomy in, no matter how you're going to do it, or a hysterectomy, were not followed.

So I think it's really important to emphasize that, yes, endometrial biopsy should be done in any woman with very irregular bleeding if your treatment for that bleeding is going to be a myomectomy or something short of a hysterectomy, including -- and I have to put in a plug here -- supra, you know, supra -- you know, we've discussed off and on here supracervical hysterectomy. And I would, you know, make the point that from an oncologic standpoint, there is great potential harm in supracervical hysterectomy similar to that of morcellation using laparoscopic or other features and that, you know, if you're going to be taking out the entire uterus, one would argue, and we as oncologists often question why would you leave the cervix, because there are you again subjecting the risk to cutting across a cancer and spreading it.

But I do think that we need to, you know, remind ourselves and our clinicians that you definitely should be doing endometrial biopsies in many, many of these women before they have uterine artery embolization,

before they have endometrial ablation. I mean, that's standard of care.

DR. DIAMOND: Dr. Simon?

DR. SIMON: Sure. I just want to offer a perspective here. So I have done uterine fibroid embolization. We've treated over 500-plus patients, maybe more. On every one of those, we've gotten an MRI prior to the procedure. In a pelvic MRI, evaluating a woman's uterus, you're looking at both the uterus and the adnexa. There's often a multitude of fibroids. It's very common that there is more than one. And the MR appearance, there'll be a multitude of sort of appearances of the fibroids as well. Some will be very characteristic, dark, well circumscribed. Others will be in varying stages of degeneration. And so I sort of want to caution or remind people that it's usually not one fibroid on the uterus. Actually, I think it's the rarity of patients where there's one fibroid or one mass.

Again, with regard to biopsy, as well, I'm not a pathologist, but have done my share of biopsying all over the body. As not a pathologist, I would say, you know, when we looked at the micrographs of fibroids and atypical leiomyomas, and then sarcoma, those aren't cytologic biopsies, which are, of course, an easier biopsy to do; it's a 25-gauge needle or smaller. Those are -- it's histology.

So these needle biopsies, if we were to, God forbid, go down that road, you're not talking about small needles. You're talking about actually doing a core. And then you have to even ask yourself if disease is

within the uterus in a fibroid, if it's a leiomyosarcoma, is it patchy, are you having -- I mean, when we even do things like lung biopsies for a lung nodule where there's a high index of suspicion, you know, we'll often say a negative finding is unacceptable until you've done multiple passes and you're really convinced that you've sampled appropriately. And so I think biopsy is a complete Pandora's Box and should be removed from the discussion. I wouldn't even go there.

In touching back on this -- so that's sort of my perspective on MR. And touching on this question, in particular, having treated many women with fibroid disease, I will echo what Dr. Iglesia and Dr. Brown have touched on. And I was really quite bothered in hearing some of these presentations. I actually went up to someone afterwards and just asked what the age of their wife was. This postmenopausal female group that ended up being morcellated, I'm really quite upset by that population of patients because I feel like someone was not really thinking about what's going on in these women; a 60-some-odd-year-old woman who presents with symptoms who goes on to be morcellated, I can't understand it. And I think we should come out very strongly, you know, at least in that demographic or that cohort that this should not be done, you know, it should be forbidden.

Anyway, those are my thoughts. Thanks.

DR. DIAMOND: Dr. Iglesia?

DR. IGLESIA: So, Dr. Yustein, I do think that, you know, we

need to have some -- I don't know if these are special controls, but some definite guidance documents in reminding practitioners about the workup for abnormal uterine bleeding. I mean, that's kind of where it starts. And working with the societies would be useful.

DR. YUSTEIN: Yeah, I think that would definitely be something that would be in the purview of the societies since that really is in the purview of practice of medicine.

DR. DIAMOND: Dr. Simon?

DR. SIMON: Actually, there's one last thing that I forgot. I was searching for words at the end there. One other thing which sort of when we look at these cases that were presented, and if, you know, if I glean something out of them like, you know, what opportunities are there to avoid these problems. One, you know, glaring issue, and it sort of doesn't necessarily always fall within the purview of the FDA, but perhaps it may have been helpful here is I was struck by the number of patients that I don't feel the informed consent for them really touched on the use of the morcellator, the impact of the morcellator on the outcome of their operation. I mean, that seemed like it was -- now, we didn't survey every patient, every family member to really explore it, but it certainly -- I was struck by that during their presentations.

And I know -- I actually sometimes get nervous when the FDA gets too deeply involved in kind of micromanaging the thinking that may take

place between a doctor and a patient. I know there is certainly a lot of discussion sometimes about off-label use of devices and should it happen, should it not happen, what are the implications, what does it mean. But, in this instance, I do feel like perhaps some attempt to push the gynecologic community to maybe make the informed consent process more significant here or approach it a little differently to ensure that, you know, these patients, they do need to be told that this morcellator is going to be used and what the implications are. And I think it may push the FDA into an uncharted area, but some attempt to kind of move us in that direction, you know, may be beneficial.

DR. YUSTEIN: So if I could just respond to that. Yes, you are correct. When it comes to informed consent, if the informed consent is during a study that's being done perhaps under investigational device exemption, IDE, it's being done as part of a clinical study for a medical device that FDA is overseeing, the informed consent is part of the IDE process, and our medical officers and teams review those informed consents very carefully. And all the elements that are put in the informed consent by the companies, which are then the ones that you as physicians participating in this study actually go over with the patients, are thoroughly reviewed by our staff here. However, outside of those clinical trials, informed consent between a patient and physician is really outside of our purview.

DR. DIAMOND: Yes?

MS. MATTIVI: So from the consumer point of view, I think the other side of informed consent is having informed consumers. And if there is a possibility -- I don't know how the FDA or what the FDA is able to do in terms of consumer education on the website, other publications. Certainly, the professional societies can also help to provide consumer education. I think the women who presented today, the families who presented today, these are intelligent people, and they're certainly capable of understanding technical information. And to have resources from the FDA, from professional organizations that they could take to their physicians and say, no, wait a minute, I want to discuss this further, would be of great benefit to the consumer.

DR. DIAMOND: Okay.

DR. SNYDER: Yeah, Dr. Snyder again. And I'm worried that, you know, we've given the FDA, you know, a list of some characteristics. And I just think ultrasound needs to be added to that. We know that its negative and positive predictive value are worse, you know, than MRI. But there are ultrasound characteristics that send up a warning sign, you know, that this is something other than usual. And I think that needs to be, you know, included as a patient characteristics, even if it's margins, you know, and so forth.

DR. DIAMOND: Okay. I would like to ask Elaine Blyskun now to come read Question No. 3, please.

MS. BLYSKUN: Thank you. So Question 3:

Given the risk of disseminating unsuspected uterine sarcoma during power morcellation, please discuss potential intraoperative mitigation strategies to reduce or eliminate this risk. During your discussion, please specifically address surgical accessories or tools, including laparoscopic specimen bags, as well as surgical techniques.

For the potential mitigations identified, please discuss:

a. The level of evidence available to support your conclusions and recommendations;
b. The level to which the risk can be reduced;
c. What, if any, risks are inherent to or introduced by the mitigation strategy itself; and
d. What, if any, additional or special training would be critical for the clinician in order to ensure its safe use/implementation.

And this is just a table to help guide the discussion.

DR. DIAMOND: Okay. So for the Panel, so what we're looking for here is mitigation strategies. That is the topic for discussion.

All right. I think -- let's let the Panel read this again, but then I think we need to move on because the issues we need to address related to this question, the specific characteristics are what is in the next slide. So everyone read that and make notes about it if you want to, and then we got to go to the next slide. Everybody set? I see a couple people still writing.

MS. BLYSKUN: This should be unchanged from the Question 3 that was previously provided.

DR. DIAMOND: Okay. So if we go to the next slide, so this is the questions that we're being asked for about potential mitigation strategies. And we're being asked for that, if we go to the next slide -- well, for each of the mitigation strategies you come up with, these are the questions that would then be asked about.

So Dr. Iglesia?

DR. IGLESIA: So I'd like to address technique in terms of intraoperative ways to mitigate risks for hysterectomies or treatment of fibroids. And I want to go -- circle back to Dr. Corrado's presentation looking at data from the Cochrane database as well as ACOG's committee opinion on route of hysterectomy, where the vaginal route is the favored route for many reasons, because it is the least invasive, and it's associated with lowest risk of injury, less amount of pain, and you can remove a specimen without morcellation through the vagina.

So to the degree that, you know, it can be done vaginally, removing it through the vagina without morcellation, which is my preferred route, and it is done in only 25% of hysterectomies in the United States, I think to some degree, we need additional training to make sure that that technique stays in the armamentarium of gynecologic surgery and we have the special skills to use it. But I have a strong, very strong opinion about, you

know, the route through the vagina.

DR. DIAMOND: Dr. Talamini?

DR. TALAMINI: Mark Talamini. I would just like to add a perspective from general surgery that Dr. Shriver would probably agree with. In GI malignancies, it is current and growing practice to take out known malignancies, including aggressive cancers, and place them in a bag and then bring them out through an enlarged incision. This is done for distal pancreatectomies for pancreaticoduodenectomy, specimens for liver cancers, stomach cancers, and others. So I think that must be included as a potential mitigation strategy, that is, putting even known malignant tissue into a bag and pulling it out through an appropriate-sized incision with no morcellation at all.

Level of evidence for that, I am not aware of any study that has randomized that practice. I'm not even aware of a study in my journal or others that has carefully examined that practice with respect to the risk of spreading tissue, but it is a common and growing practice among GI and oncologic surgeons in general surgery.

DR. DIAMOND: Dr. Isaacson?

DR. ISAACSON: Just a little bit difference between the types of cancers that you're referring to and the fibroids. The fibroids, often when they're symptomatic, as you know, are between -- oh, they can be 8, 10, 12, 15 cm in diameter, and they're solid. And there really is -- if you're going to

say you're not going to morcellate even in a bag, then there's no reason -- you just make a regular laparotomy incision to get it out. I mean, so it's a really -- it's a different animal. It's not the same thing as a colon cancer. It's not the same thing as a pancreatic cancer. These are large, solid, hard, rubber ball tumors. So if you're going to remove it, anything other than a laparotomy, it does require morcellation even vaginally.

The majority of the fibroids that we're talking about are not fibroids that can be brought out through the vagina without morcellation. And, again, morcellation to me is -- morcellation is morcellation is morcellation. Doesn't matter if it's power morcellation or if you're using a knife. I don't know that there's any difference in spillage there.

So should we use a bag to mitigate the risk? I think that's open for discussion. I think that's a really good question. And I think, as we know, there are potential risks of using a bag, not the spillage risks, but just the training that's necessary, the lack of visualization, other parts. And that's going to require quite a bit of work. And that's another discussion.

But I think as far as getting back to this question in my mind, good surgical principle and technique is crucial. And I think if you have any tissue spillage, whether you're doing it through a myomectomy where you're not taking out the uterus, so it's uterine-sparing, so in my mind, even if you have -- take out an intact fibroid, you have damaged that -- or you've injured the uterus, as we've heard this morning. You know you're going to spill. So

what do you do afterwards? You irrigate the best you can, make sure that there's no visible chips behind, and as you're irrigating, I know there can be some microscopic cells behind, but it's as few as possible. So I think, again, teaching that technique whether you morcellate or whether you do it open is crucial, and it will help mitigate the risk.

DR. TALAMINI: This is Talamini again. Just to respond. I agree completely that they're different animals, but just with respect to the question of whether a bag is an effective containment strategy for malignant tissue in general, the experience from GI surgery and GI malignancies would say that a bag can be an effective containment strategy absent morcellation.

Now, in general surgery, sometimes taking out spleens, we'll put them in a bag and then morcellate them with an instrument under direct vision, again, using a bag as a containment strategy. So, again, my point is just that from another specialty, a bag can be used to contain malignant tissue.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: So, first, just to add to what was just said, what Dr. Talamini said, we have evidence from the specialty of gynecologic cancer and gynecologic oncology that you do not need to put a known cancerous specimen in a bag. You know, the vast majority of the known endometrial cancers, including uterine carcinosarcomas, including known leiomyosarcoma, at my institution and in my practice, if the patient meets

the other criteria, we do choose minimally invasive surgery because it is better for that patient in terms of significant outcomes, and we remove the specimen through the vagina.

I do think that, you know, again, the best thing to do is not to chop cancer up. No matter how you chop it up, it's better not to chop it up by taking off the top of the uterus. Again, supracervical hysterectomy is, in my opinion, as big an issue, if not a larger one. Many more patients do we see in our practice who've had supracervical hysterectomies and have a leiomyosarcoma or endometrial cancer, you know, there's -- in my opinion, there is no Level I, II, or III evidence to support the increased risk associated with supracervical hysterectomy versus risk of undiagnosed malignancy.

So I think that we know that you can take uteruses out through the vagina without a bag even if they have cancer in them as long as they are intact. But I would focus on a technique of, again, of avoiding any type of morcellation when you're doing a hysterectomy and/or removing a fibroid. And in my experience, the best orifice or potential orifice to get that out is going to be through the vagina.

And we have prospective, randomized large study that was done over many, many years in endometrial cancer comparing open surgery, including lymph node staging, to laparoscopic surgery and lymph node staging. Bags were not used even for the lymph nodes that were removed, and there was no increased risk of vaginal, abdominal, or any type of

recurrence in the women who were randomized to having laparoscopic surgery. So that's just some information.

So I think that intact laparoscopic removal through an adequate orifice is the best surgical technique to avoid spillage of any type of unsuspected malignancy, including ovarian, tubal, endometrial, or sarcoma. And I think there's good evidence to support that.

DR. DIAMOND: Okay. Other comments from the Panel?

Dr. Fisher?

DR. FISHER: Fisher, FDA. This question is asked with the naivety of a nonsurgeon. Dr. Sobolewski showed some pictures yesterday of these huge fibroids. And Dr. Talamini was talking about possibly containment with a smaller, smaller organ and getting them out. So my question, and I know it's not going to be this simple, but my question is does size ever play into the equation or could it play into the equation that -- and I don't know if there's anything out there, any guidelines that are followed now with number of fibroids, size of fibroids, or anything like that, that would influence your decision as to how you would take them out?

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: So I'll answer that question in full -- not a conflict of interest, but I am an examiner for the American Board of Obstetrics and Gynecology in both general, OB/GYN, and gynecologic oncology. And that is a common question. It is really -- this is something that

is expected that someone is adequately trained and board certified in the specialty has developed the ability to assess and appropriately apply their level of skill to what size fibroids, adnexal masses that they are going to use either a minimally invasive approach or an open approach. And I emphasize that obviously included in that minimally invasive approach may be the use of morcellators, but absolutely size is an issue.

I have operated on patients with known endometrial cancer and known fibroids who were told by other surgeons I could only do it abdominally, and I've done it as a minimally invasive procedure without morcellating.

But, unfortunately, there is no exact prescription or be able to say a certain size, but that is definitely something that the surgeon should be considering, what is their experience, their ability in terms of size. And there's certainly in the case that we were shown by the family member, again, when you have a 20-week size uterus, the value or why someone would consider morcellating that is really open to question, because again, yes, I don't know too many -- you cannot get a 20-week-size or 24-week-size uterus out through any orifice without morcellating, so --

DR. DIAMOND: Dr. Isaacson?

DR. ISAACSON: So I think I need to clarify some of the things that you've said. So you're suggesting that any fibroid that's too large to be extracted through the vagina, so let's say it's 8 cm or greater, there's no

other way to get this fibroid out other than morcellation? I missed your point regarding that.

DR. CAROL BROWN: I did not say there was no other way to get it out other than morcellation. I was answering the specific question, what is the best surgical technique to minimize the risk of intraperitoneal spread of unsuspected sarcoma, but I extended it to any unsuspected malignancy. That's what I'm specifically answering about. That's the best way to minimize the spread of malignancy. I'm not saying what's the best way to do a myomectomy or take out a fibroid.

DR. DIAMOND: Other comments from the Panel?

DR. IGLESIA: And Dr. Fisher, I don't think there is an upper limit. I don't think there is a lower limit. I think that it requires some good clinical judgment, and there's no shame in making the incision, but if there's a high -- of suspicion in a woman who's having irregular bleeding not worked up with, and maybe you get an MRI for that person and still not sure, that person better be told that there is a potential for that risk, for that being an undiagnosed cancer and the potential for having an adverse outcome from doing morcellation. You know, it's the being able to diagnose this preoperatively to preempt the bad outcomes. That's really at the heart of the matter, in my opinion. So, you know, that's sort of where a lot of guidance is needed, because I feel like there's been -- we've failed some patients here.

DR. DIAMOND: Dr. Yustein?

DR. YUSTEIN: So, Dr. Diamond, maybe if we can push the Panel a little further, let's take this scenario where a surgeon has decided to perform morcellation with the device on a fibroid. Can the Panel give any comments on their level of confidence that we have any ways to mitigate the risk assuming that we are performing intraperitoneal power morcellation, okay? So we're not talking about removing something in a bag intact. We're not talking about vaginal hysterectomy. We're talking about somebody has decided to do intraperitoneal laparoscopic power morcellation.

Are there any items, any mitigation strategies at that time, including whether or not you have confidence in bags or a particular surgical techniques like the ones described by Dr. Serur -- I don't know if I'm pronouncing his last name right, S-e-r-u-r -- where he puts it in a bag, brings it up through an extended port incision, morcellates above the abdomen -- I kind of described that briefly during my talk yesterday. Are there any techniques or the use of the bag in that situation? You've already decided you're going to morcellate. Does the Panel have any confidence or any data, thoughts on that data, in terms of the ability to mitigate the risk of dispersing cells throughout the abdominal cavity in that situation?

DR. DIAMOND: Okay. Dr. Isaacson?

DR. ISAACSON: Intuitively, I think that's a good idea, and I think it should be recommended. I think that --

DR. YUSTEIN: What is it?

DR. ISAACSON: That putting it -- morcellating -- if you're going to morcellate and it can be done safely in a bag, that that should be encouraged. The caveat is doing more work to study the bags, number one, and study the techniques, how easy it is to train and convey those techniques so it can be done safely, and then here's our opportunity to start from scratch and actually gather data on the potential risks of that technique as well. But I still believe intuitively, and that's all we have is intuition here, that it will likely mitigate the risk of upstaging a tumor if you morcellate within a containment system such as a bag.

DR. DIAMOND: Other comments? Oh, I'm sorry. Dr. Shriver?

DR. SIMON: But that's the problem. After 20 years, all we have is intuition. There's no evidence that bags or any containment devices prevent the outcome we're trying to prevent. So stopping where we're at, banning the devices, and in the context of a future -- that's a great question for a clinical trial. That's exactly how it should be asked. You could have two arms, one without a bag and one with a bag with a next generation technology and containment technology and extraction technology. So that's a perfect setup for what's needed after 20 years of we're on intuition still is a clinical trial with a next generation device.

DR. DIAMOND: Go ahead, Dr. --

DR. IGLESIA: Cheryl Iglesia. I don't think that the bag would be

the be-all, end-all here. And, quite frankly, even when I looked at the really nice elegant video, I looked at that size of the uterus that was in that bag, and I thought to myself, well, that could have come out through the vagina. So I think that there are complications that can come with the bag in terms of visualization, in terms of -- you know, Keith was just talking about, you know, the mentioning incarcerated hernias that occur after the use of that. So I don't want to -- I don't -- while intuitively, it does make sense that it would prevent spill, I do think that we need to try to minimize the use of morcellation where possible. And there might be some cases where you've decided to do it, and intuitively, the bag would seem to have less spread. But in that particular patient, which probably was going to be the minority, make sure you have the adequate workup, make sure that patient has been told that a morcellator is going to be used and the risks of morcellation, including the risk of -- whether it be 1 in 350 or whatever -- an undiagnosed malignancy when there's a fibroid present.

DR. DIAMOND: Actually, I think Dr. Gallagher was next.

DR. GALLAGHER: I just want to say the idea of doing a clinical trial to kind of figure out that intuition kind of question is certainly intriguing, but I think I would also caution just to say a lot of bench work would have to be done before that could happen, because the bags we have right now, we don't know that they actually work for that purpose. So I wouldn't want us to jump the gun and make a suggestion saying let's move to clinical trial before

doing bench work. Thank you.

DR. DIAMOND: Okay. Dr. Wentzensen and then Dr. Talamini, please?

DR. WENTZENSEN: Yeah, I also, along the same lines, I don't think we have seen any convincing evidence that it can be mitigated, and I think any suggestion or even intuition would be misleading. So I would want to be careful in any statement here. But I'm not exactly sure how that clinical trial would look on the other hand because you -- I don't know what endpoint you would want to go for. I mean, a safety endpoint would require a huge number, and that there would be ethical questions raised, so I don't know how this would work, but that's a side comment.

DR. DIAMOND: Dr. Talamini?

DR. TALAMINI: This is Talamini. I just have two additional comments. In Question 3, it says, "unsuspected uterine sarcoma during power morcellation." And I think one of the things you're hearing from the Panel, obviously, the power morcellator is the thing that you regulate. But the real issue is cutting across this tissue. I think you've heard that over and over again. And it's easy to get the two confused, but there's an important principle there.

The second thing is, point b, is the level to which the risk can be reduced. I think the other thing you're hearing is that, based on the uncertainties, the risk cannot be reduced to zero.

DR. DIAMOND: I'm sorry. Dr. Brown? Thank you.

DR. CAROL BROWN: Carol Brown, with respect to the bag, as you may have guessed, I already have concerns about unintended consequences, unnecessary procedures. So if we estimate that there are 25,000 to 50,000, which I think we heard somewhere today, uses of laparoscopic power morcellators to either accomplish a hysterectomy minimally invasively or a myomectomy minimally invasively, so then we would be saying, based on, unfortunately, really no good evidence, that basic scientific evidence looking at the transmission of the cancer cell across whatever the barrier is that it's made out of, et cetera, that we're going to say that every woman who has the use of a laparoscopic power morcellator to remove her fibroid or her uterus, you have to use one of these bags, that's a whole new technique. I had the same reaction as Dr. Iglesia looking at that video, all due respect. I mean, that uterus could have come out through the vagina.

And the other thing that I'm very concerned about when I looked at that video, my concern is that, wow, the small bowel is right there through a little thin plastic, and someone is going to be sticking a sharp, rotating object in there. And, again, I go back to my concerns that were raised when I saw those six women in the MDRs who died because that rotating thing chewed up their arteries and they died on the table. I personally would be very concerned and would want to see a clinical trial

showing that the bag doesn't increase the risk of those other types of problems. So I do not think that we have evidence that the bag will mitigate the risk.

DR. DIAMOND: Okay. So I'm going to try, then, to summarize what I think I've heard around the table. First of all, that there are some techniques, such as vaginal surgery when it's possible for removal of an intact uterus, that would be a mitigation strategy that could be utilized; concern with supracervical hysterectomy and potentially cutting across a tumor; that multiple individuals mentioned the desire to avoid any kind of morcellation of tissues and to remove the specimens intact. There was a lot of discussion about the use of bags, and while it was thought that, intuitively, that that may have advantages in reducing dissemination of an unrecognized malignancy, the data to support that appears to be totally lacking at this point in time. And I think, therefore, the conclusion is that we don't know through the use of the bag to what extent, if any, we're able to reduce the risk at this point.

Is that a fair summation, or does anyone want to add something to that?

(No response.)

DR. DIAMOND: Dr. Fisher, Dr. Yustein, are there other components to this question other --

DR. IGLESIA: I have one other thing to say. I think we may

answer this in the next question -- Cheryl Iglesia -- about the subtotal hysterectomy, Carol, you know, and Dr. Sobolewski alluded to this yesterday, this is a very low-risk population. With the prolapse and a normal-sized uterus, postmenopausal, you may do a supracervical just because it's a better point of attachment for mesh and may decrease the risk of vaginal cuff aversion of mesh. And, you know, and for that technique, some people do use morcellators. I'm just saying that is something that I think we might be talking about in further questions about benefits and risks specifically to that, but I'm going to just preempt myself, I guess.

DR. DIAMOND: Okay.

Other additional comments from the Panel to my summation?

Dr. Fisher, Dr. Yustein, anything else you want us to add to this question or -- all right. Then we'll ask Elaine Blyskun --

DR. FISHER: Yes, if I --

DR. DIAMOND: Okay.

DR. FISHER: Just clarification on your summation there, are we saying that the Panel has said that they are -- that no one is in favor of morcellation of an unsuspected sarcoma or that they're not in favor of morcellation of a fibroid?

DR. DIAMOND: What I heard around the table is that they're concerned about morcellation regardless of how it's being done.

DR. FISHER: Thank you.

DR. DIAMOND: Again, anyone have a different -- I don't see anyone disagreeing with that as to the consensus. Dr. Isaacson?

DR. ISAACSON: I think it's a little different.

DR. DIAMOND: All right.

DR. ISAACSON: My point was that I don't think there's a difference in the risk of morcellation whether it's power morcellation versus any other type of morcellation. That's not to say that there is no role for morcellation whatsoever. So that would be my sum. That's a little different.

DR. DIAMOND: Yeah. Okay. Dr. Snyder?

DR. SNYDER: Dr. Snyder again. And in your summation, you know, I heard about, you know, that there's, you know, no data for the mitigation of spreading, you know, an occult malignancy. But the second point Dr. Brown made is that we also don't have evidence of the safety, you know, or increased risk associated with morcellation itself --

DR. DIAMOND: Whether there was an increased risk?

DR. SNYDER: Right.

DR. DIAMOND: Yes.

Dr. Brown?

DR. CAROL BROWN: So, Dr. Fisher, just to clarify what you said, so I'm answering this question, everything that I just said, I'm answering about directly what can be done to reduce or mitigate the risk of spreading intraperitoneal malignancy in terms of your surgical technique in unsuspected

sarcoma. I was not saying those things about what's the best way to do something for an -- you know, when you're doing a myomectomy or vaginal vault suspension. I'm specifically trying to answer the question, which I thought we were specifically talking about how to reduce or mitigate the risk or eliminate the risk of disseminating unsuspected uterine sarcoma.

DR. DIAMOND: Dr. Gallagher?

DR. GALLAGHER: To address Dr. Fisher's question, I'm an ethicist, not a physician, so I don't usually talk about -- when we think about what the principles of ethics are in medicine, we rarely hear about the principle of nonmaleficence being so important. And nonmaleficence is kind of the principle out of which the "do no harm" comes from. And I think for this particular question, I think that principle of nonmaleficence, meaning we want to avoid harm to the very best of our ability -- and it's really not necessarily avoidable all the time, right, it's not a zero sum -- combined with a principle of justice, specifically that of what does society owe to one, which is why the FDA is doing what it's doing, I think as an ethicist, I don't believe at this moment that morcellation for the purposes that we're talking about today, not for other things, but for this particular thing, is something that I would support.

(Applause.)

DR. DIAMOND: Okay. We'll now ask Elaine Blyskun to come read us the next question, please.

MS. BLYSKUN: Thank you. This is Elaine Blyskun. So we're going switch up to Question 5. This is revised from what has been provided to you previously, so it reads:

Please discuss whether there are specific populations or clinical scenarios in which:

a. The benefits of laparoscopic power morcellation outweigh the risks and offer clinical utility. If so, please describe the patient populations, the necessary risk mitigations to maintain a favorable benefit/risk profile, and the rationale for your response;

b. The risks of laparoscopic power morcellation outweigh the benefits regardless of whether mitigation strategies are employed. If so, please describe the patient populations and the rationale for your response.

Following your discussion of women considering laparoscopic hysterectomy, please provide responses to 5a and 5b for women considering laparoscopic myomectomy where power morcellation would be used.

Thank you.

DR. DIAMOND: All right. And we're going to try to answer these first (a) and (b), so if we could go back to question (a), please? And for the Panel, these questions are on this sheet that was passed out maybe 30 minutes ago. So look at the slide version as opposed to the other versions of

the questions that you received.

All right. So the question we're being asked is benefits of laparoscopic power morcellation, what are the patient populations in which that's so, and necessary risk mitigation to maintain a favorable benefit/risk profile. Who from the Panel would like to start?

Dr. Isaacson?

DR. ISAACSON: Let me give you a specific patient population. This is a 25-year-old who's had two-year history of infertility, has multiple uterine fibroids, has no other known risk factors for leiomyosarcoma that have already been discussed, and is having heavy uterine bleeding -- symptoms, and wants to desperately have a family. Therefore, she wants a uterine-sparing procedure. This is one in which I would look, after a complete workup has been done with the assumption -- including the appropriate biopsies, if necessary, MRI, if necessary, what have you, based after the ultrasound, and I would give that patient an option saying you have an option of we can do a open myomectomy in which we will eliminate the risk of upstaging your -- I shouldn't even say we'll eliminate the risk -- we may minimize the risk of upstaging your cancer or we can offer a laparoscopic approach with morcellation technique, which may include power morcellation. So that, to me, the benefits of -- in a young patient who wants to maintain fertility so it could reduce the risk of postoperative adhesions and get her back to trying to proceed with her quest for a family as soon as

possible, that would have a favorable benefit/risk profile in my mind.

DR. DIAMOND: All right. And if I'm reading this question, so that's a patient population that you would think of that. Are there necessary risk mitigations that are needed in that population?

DR. ISAACSON: Well, again, this gets back to the, number one, the informed consent saying I'm not eliminating the risk that this could be a sarcoma even if it's a 25-year-old, though I think it's -- you know, I'll give the best information I can give. And, again, we could -- I would discuss the risk/benefit, and we just don't know yet about using any type of containment device. But, otherwise, the use of a power morcellator in that particular patient I would think would be a reasonable option if that's what she chose.

DR. DIAMOND: Okay. Dr. Iglesia, it sounded like you wanted to say something.

DR. IGLESIA: Well, I agree about that infertility patient, and that would be a clinical scenario appropriate to a low-risk patient. The other one, as I mentioned, is the prolapsed patient in a normal sized uterus who needs mesh. And in order to do a subtotal hysterectomy, you have to -- and attach the mesh, you're not going vaginally, so you know, morcellation is a technique that is less invasive, and in that particular scenario, the benefits may outweigh the risks.

DR. DIAMOND: So this would include those women without fibroids?

DR. IGLESIA: You know, 80% of women have fibroids, so, you know, it may not be clinically significant, but there might be a small myoma in there. It's low risk. And this is where the clinical judgment, you know, comes in -- it's a woman who's postmenopausal, most likely, 60-year-old woman, yeah. She has a history of fibroids, and they've shrunk, and she's having no postmenopausal bleeding, but her uterus is hanging out halfway between her legs. And you want to add a mesh, she's worried about the mesh, you know? Some people use that technique, although there are vaginal approaches for prolapse, and there's vaginal mesh, which is a whole ball of wax in and of itself, and there are native tissue repair options. There's Level I evidence that the sacral colpopexy has the highest cure rate and the highest reoperation rate. But it involves a mesh use. And with a mesh on an open cuff, then you have the complication, which is anywhere from 3 to 5% of having a mesh exposure on the cervix.

So, in that particular scenario, having a morcellator out on a low-risk population -- and this kind of mirrors the position statement that was presented in our packet by the American Uro-Gyn Society -- that particular patient may have a favorable benefit/risk profile.

DR. DIAMOND: Dr. Snyder?

DR. SNYDER: In the last question -- I mean, the last sentence in this is risk mitigation even in that patient, you know, that we just heard about, you know, that's going to have a supracervical, and it would include

pap and some sort of assessment to rule out endometrial adenocarcinoma.

DR. IGLESIA: Right.

DR. DIAMOND: Dr. Afifi?

DR. AFIFI: As a non-clinician here, I have a question in my mind, and I'm wondering if the clinicians here can answer it. Is it possible ahead of time before doing -- before any intervention is done to answer the following question: Is this fibroid or uterus possible to remove with a minimally invasive procedure without the need for morcellation? Okay. In other words, can you, for example, determine that the fibroid is small enough so that you know you can do a minimally invasive process to go in and get it out without the need for morcellation?

DR. CAROL BROWN: So I'll answer that, and then I'll go ahead and answer Question 5. Yes. But, again, there is no one right or wrong answer. This is a matter of surgical skill, surgical training, the tools you use, the way -- you know, so there's no -- there is nothing that the FDA can regulate about that. If that's really such a huge problem, then that's our fault as surgeons in gynecology for not training people correctly and not making sure that they follow basic principles.

So to answer the question, the first part of the question is about hysterectomy. So are there benefits of laparoscopic power morcellation outweighing the risks for hysterectomy? I have to confess that, again, for me, as a gynecologic oncologist, it is hard for me to think of a

clinical situation other than the one that Dr. Iglesia just made me aware of where there might be a benefit of a supracervical, or leaving the cervix in, to allow attachment of mesh in a woman who has severe prolapse. That's the one exception, but other than that, I think that there is no evidence to support leaving the cervix in. And, therefore, other than what she just mentioned, it's very hard for me to think of a clinical situation where a woman needs a hysterectomy, meaning removing the entire fundus of the uterus, because my bias, again, trying to completely mitigate the risk of spreading undiagnosed cancer, not just leiomyosarcoma, but also cervical and endometrial cancer and ovarian and tubal, is to not morcellate. And there, the size and the presence of fibroids will be an issue. And yes, I may be able to get a 18-week-size uterus out intact through the vagina in someone who's had six kids. And my colleague my not. So my answer to (a) is I really can't think of other than the situation she just mentioned.

My answer to (b), yes, I can think of -- describe the situations where the risks of laparoscopic power morcellation outweigh the benefits. Again, perimenopausal women where the fibroid is growing, she has abnormal bleeding. Even if you think you've excluded the reason for abnormal bleeding, if she's postmenopausal, I don't see a justification. Particularly if you're going to take the whole uterus out, why would you leave the cervix in? To me, that's not acceptable.

And then Dr. Isaacson, I think, answered this question with

regard to myomectomy, not hysterectomy, but we're supposed to answer it with regard to myomectomy, and I'm going to have to say I can't answer that because I really -- I don't do myomectomies myself because, in general, unless it's, you know, for the reasons he said, but for me, those at-risk patients, perimenopausal, you know, I kind of have a bias. Only reason you should be doing a myomectomy is if the woman needs to keep her uterus for a very good reason. So I can't really answer this question with regard to myomectomy. But I think Dr. Isaacson did, and maybe some of the other clinicians could address the myomectomy issue.

DR. DIAMOND: Okay. Other members of the Panel have a comment?

Dr. Simon?

DR. SIMON: It's actually a question for Dr. Iglesia. In that scenario you describe of a woman really complaining of prolapse, normal size uterus, but if it indeed is a normal size uterus, to do the supracervical hysterectomy and then remove the tissue, would you still need to use a morcellator, or is there a way just with a mini-laparotomy or some other means to get that tissue out if it's a normal size uterus without necessarily -- so you're not doing a vaginal hysterectomy, obviously. So but does the morcellator -- is it necessary to use the morcellator to get the tissue out, then?

DR. IGLESIA: Oh, clearly, it's not necessary, but it's a time

saver. That really is --

DR. SIMON: Okay.

DR. IGLESIA: This is a very long operation already in terms of all the dissections and the anterior and posterior -- they have to do with it, the sling that you have to do with it, you know, the dissection in the pre-sacral area. But, obviously, you can make an incision and do -- in the posterior cul-de-sac and take the uterus out through there. To be quite honest, I like vaginal surgery. I'll still do vaginal hysterectomies and then do a laparoscopic colpopexy, you know, and that's the scenario that we've described as well as an option. But there are some people who prefer all endoscopic approaches. You know, it isn't something that I do on a regular basis.

DR. DIAMOND: Other comments?

Ms. Aronson?

MS. ARONSON: I have a question about the young population that may be dealing with infertility and sort of the requirement of appropriate workups. We're assuming that there's going to be all these appropriate workups done, so that's where I get a little concerned that it doesn't always happen. But also I read about parasitic growths. And I was just wondering -- so this is benign fibroids that might be found. And would parasitic growths also cause problems for future infertility with the power morcellation?

DR. ISAACSON: Parasitic growths, you're right, they do occur. But I've never seen any data that they occur more frequently as a result of any morcellation versus a standard open myomectomy. So that has been a problem long before we did laparoscopy. There were still instances of parasitic growths just from doing a myomectomy. So I think it's a risk with both procedures, but I don't know that one is a greater risk than the other.

DR. DIAMOND: Dr. Mattrey?

DR. MATTREY: Yeah. I just need clarification. There were a lot of numbers thrown around yesterday and today. Is there evidence that the risk of spreading either benign or malignant tissue is similar between morcellation and myomectomy? I mean, the minute you injure the tumor or the uterus, is the risk somewhat equal or is it a lot worse with morcellation?

DR. ISAACSON: I don't have that answer either.

DR. DIAMOND: Okay. Dr. Brown?

DR. CAROL BROWN: Carol Brown. So I can address that as a gynecological oncologist who operates on these patients that have had either myomectomy or supracervical hysterectomy or laparoscopic power morcellation and then they've been told they have leiomyosarcoma.

So I can tell you that, you know, when we think about going back in, we are going to be more concerned if there was laparoscopic power morcellation or any type of intra-abdominal morcellation, if you did it with a knife, if you did with a bovie, that there will be more likelihood that there

were pieces of the mass left behind than if you did a myomectomy. However, and I looked at this again last night, when you go through all of the studies that do include myomectomy, there really is nothing to suggest that the risk would be less of actually causing spread. Maybe it is less likely you're going to go right back in and see gross tissue, but in terms of their being microscopic cancer cells that have escaped and have implanted in the peritoneum and will ultimately grow, I think from oncologic principles, you have to assume that the risk is equal. And, again, that's why I'm emphasizing I put into the same category myomectomy and supracervical hysterectomy as a risk of causing future intraperitoneal spread.

DR. DIAMOND: All right. Not seeing any other -- oh, Dr. Fisher?

DR. FISHER: I'm not going to let you get off the hook. There has been a term that has been tossed around over the past couple of days. It's risk stratification strategies. And my guess is that you use these for trying to identify low or lower risk populations. So I'd like to get the Panel's opinion on if this would have utility. And if you believe so, how would be the best way to proceed in trying to do something like this?

DR. CAROL BROWN: Could you please clarify the question? Risk reducing strategies for --

DR. FISHER: Risk stratification strategies.

DR. CAROL BROWN: Stratification of risk of what? Of a woman

having an unsuspected sarcoma?

DR. FISHER: Right now, we'd use it kind of -- I don't have anything specific. I would use it in terms for power morcellation. You know, I've heard a couple examples of fertility sparing. I heard special indications. So in just general terms to kind of help us with are there subpopulations of individuals that could benefit from morcellation or have a low or lower risk due to the procedure? And I'm just tossing it out as a general question.

DR. IGLESIA: I mentioned this on the first day that we'd love to see when you're having a one-on-one conversation with your patient, we'd love to be able to have -- I think a lot of practitioners would love to have a tool where you're not quoting a 1 in 350, 1 in 10,000 rate when you're here talking to a woman with fibroids. But you take her individual personal characteristics, you know, and when I was saying a risk calculator, I was referring to what the risks are of potential leiomyosarcoma in a fibroid based on her history. So, you know, African Americans, three times more likely. Obviously, older, much more likely. Those genetic HLN and renal cell and retinoblastoma and BRCA, you know, much more likely.

But, you know, that's why I thought we've got the data out there. We've got the SEER database. We obviously need more bench research, but you know, to get genetic testing, or our colleague from the Mayo Clinic was talking about different chromosomal abnormalities, whatever it is, I mean, it would be nice to have that just so to say, Mrs. Smith,

you know, your risk is X of this, and you know, in this particular situation, hysterectomy, whatever, open would be recommended, you know? There might be ways that you can have that conversation to personalize it.

DR. DIAMOND: Okay. Dr. Talamini?

DR. TALAMINI: So, again, borrowing from another specialty, the Society of Thoracic Surgery has an app which can very precisely predict the risks for cardiac surgery given a set of criteria that the surgeon or a patient can punch in live. Now, with respect to this one issue of power morcellation in an unsuspected leiomyosarcoma, that would be exceedingly difficult to do. But in this entire realm that we've been talking about, with a robust dataset, which the Society of Thoracic Surgery sought to get over the last 25 years, that certainly is possible.

DR. WENTZENSEN: Yeah, I want to pretty much say that same thing from a different angle. We're using that for cancer risk prediction and for screening guidelines, and there is an app that can give risk. But it's based on millions of women with large numbers of outcomes. So I think although we all have a gut feeling, there's no way we can come up with a reasonable approach to do a risk calculator for this question at the moment.

DR. FISHER: Okay. And -- oh, I'm sorry.

DR. CAROL BROWN: Carol Brown. I actually take a little bit of a different take. I don't think that we need a genetic test or a fancy anything to know. I think that we are already equipped with the basic clinician

judgment and training to know, you know, what is the appropriate situation to consider a myomectomy and to consider morcellization, however you're going to do it, for anything. You know, again, Dr. Isaacson described the type of patient. I don't think we have to confirm that that type of patient is appropriate to have a myomectomy using morcellation or however you're going to do it because that patient already, given the clinical characteristics, is in such a low-risk category that you don't need to add on some other -- that there's no -- at my institution, we developed a risk calculator for women who have uterine leiomyosarcoma in terms of their risk of recurrence and prognosis, et cetera. But, again, it's just not possible to do it on the basis of what fibroids are fibroids versus uterine leiomyosarcoma. It would take, you know, 20 years of collecting every hysterectomy and following them. It's not feasible. But I don't think you need that.

DR. DIAMOND: Ms. Mattivi?

MS. MATTIVI: Again, from the consumer standpoint, I think many consumers probably at this point, with the volume of information that we don't have, would even be happy to know is my risk higher than average or is my risk lower than average? Do I fall in the upper quartile of the risk scale. You know, they don't need an exact number of my risk is 1 out of whatever. People, a woman would just want to know do I have a higher than average risk for this happening?

DR. FISHER: So, Dr. Diamond, I'm sorry, I didn't mean to get

too far off track there. But if that little discussion spurs somebody out there to progress down that pathway, so be it.

DR. DIAMOND: Okay. All right. So unless someone else has a comment, then I'm going to sum up what I think are our responses to Question 5.

And the answers are, first of all, looking at it from the point of view of an individual that will be undergoing a hysterectomy, there are -- there is one situation where -- we've been identified where there may be a benefit of morcellation, and that is the individual who has a urogynecologic condition for which a mesh is going to be placed at either the cervical stump or the vaginal cuff. And in order to reduce the risk of erosion at a later time, having the cervical stump there may be a benefit for those individuals and the use of morcellation to remove the uterus.

We have identified multiple times patient populations in whom the risk would be more than the potential benefit, and those go again to the patient classification characteristics and imaging findings that we've described in response to earlier questions.

With regard to myomectomy, the one example where there may be a benefit is the young infertility patient who desires to preserve her fertility potential, and that individual may have a benefit of resection by morcellation of the fibroids. But in other populations, the risks may exceed that of the benefits.

Is that a reasonable summary of our discussion?

Dr. Isaacson?

DR. ISAACSON: That's a terrific summary of the discussion. But I had one other point that was outside the discussion.

DR. DIAMOND: Okay.

DR. ISAACSON: And just to clarify that we really haven't touched upon uterine conditions unrelated to fibroids, specifically, on enlarged uterus from adenomyosis in which an MRI has been done and there is absolutely no evidence of any fibroid. As the chair, do you suggest we discuss that situation or is this just -- would you like to just limit it to fibroids in general?

DR. DIAMOND: I guess I'll look to the FDA in whether you want discussions about hysterectomies in general or, more specifically, related specifically to fibroids?

DR. YUSTEIN: Hold on. I'm getting several people in my ear at one time. So I only have two ears.

DR. DIAMOND: So the question was, was there other uterine conditions such as adenomyosis was --

DR. YUSTEIN: Okay. So, originally, when we were running short on time, this question was actually split into three, and we wanted the Panel to focus on patients who present with fibroids as the primary diagnosis. The second component of that was patients who present with primarily other

presumed benign conditions other than fibroids, i.e., adenomyosis or endometriosis or pelvic organ prolapse. And the third one was going to be patients with known or suspected malignancy. So if we have a little extra time -- I don't know how we're doing on time, you know, we started going down that road. Dr. Iglesia was talking a little bit about the pelvic organ prolapse patient subsets, and we started going down that line. We didn't talk about some of the other benign conditions, but if people want to talk about, that'd be great.

The other thing that we would like the Panel to do is, so far, what we've heard is kind of on the edge, on the various extremes, in terms of young patients seeking myomectomy and then kind of the perimenopausal or menopausal woman. But what about that group of patients in between, your average woman, you know, who comes in at 30, 35, 38 years old with fibroids. We haven't really touched on are there situations where the benefits outweigh the risks and the risks outweigh the benefits. So we kind of touched on the older patients who are peri or menopausal and the younger ones who are seeking fertility -- seeking surgery for fertility issues. But can the Panel address benefits and risks and risks and benefits for just your average woman who's, like, in her -- and I don't know if that's average, but in her 30s with fibroids who's coming in who's premenopausal, you know?

Anyway, so I'll leave it up to you, Dr. Diamond. We'd like at

least that part addressed. If there are other parts of patient populations other than pelvic organ prolapse where we want to talk about adenomyosis or endometriosis, et cetera, we'd be more than happy to hear the Panel's discussion on that, too.

DR. DIAMOND: Okay.

DR. YUSTEIN: Did I answer your question or not?

DR. DIAMOND: Yes, I think you did.

DR. YUSTEIN: Okay.

DR. DIAMOND: So let me go into the one scenario that you just described of a known or suspicious mass, would any of the Panel recommend morcellation. I think what I've heard over the last two days is that I think everybody would say, no, they would not. Is there anyone who would disagree with that?

Dr. Brown?

DR. CAROL BROWN: Yeah, I just want to clarify that because Dr. Talamini mentioned that there are certain other cancers where you deliberately, knowing you have cancer, morcellate and use a bag. And, again, I just have to emphasize that for GYN, for the uterus, we don't do that. I mean, if it's so big that you have to chop it up and you know there's cancer, you don't chop it up.

Sometimes when we do -- in order to remove ovarian masses that we may be suspicious are malignant, we will put those in a bag. So I

would say that we should very strongly say you should not use any type of morcellation of a suspicious or known gynecologic malignancy. No question.

DR. DIAMOND: Okay. Dr. Isaacson and then Dr. Talamini.

DR. TALAMINI: Could I just clarify --

DR. DIAMOND: Dr. Talamini first, then Dr. Isaacson.

DR. TALAMINI: So just to clarify, what I was trying -- I probably misspoke -- I was trying to say there are examples where we put known tumors into a bag and don't cut across them --

DR. CAROL BROWN: Oh --

DR. TALAMINI: The example that I did give was spleens, where we don't suspect a malignancy. So it's a little bit different than that principle. So, hopefully, that clears that up.

DR. DIAMOND: Okay. Dr. Isaacson?

DR. ISAACSON: Yeah. Just to address your question on a woman who's in their mid-30s, again, age sometimes is not as crucial as whether or not they want to preserve their fertility, because as a reproductive endocrinologist, and I'm sure Dr. Diamond sees the same thing, the majority of the patients I see who do want to get pregnant are between the age of 35 and 42. So that is a large population in which they don't want their uterus removed and in which the minimally invasive approach, no matter how you do it, will result in fewer adhesions and a better reproductive outcome.

So, again, I gave the example, an obvious example of a 22-year-old who may be on that low end of the spectrum at risk for sarcoma, but the majority of our patients really are in that 35 to 42 years of age for fertility who are requesting -- who have this type of surgery need.

So, again, I think if I looked at that patient, and I -- again, I would give as much information as possible to the patient that I have, as accurate as it can be, and go over the risk/benefit of the various approaches.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: Sorry. I have to add a corollary to that, because I think we have to be cognizant that now there are women who want to hold onto their uterus for their own reasons. They are absolutely convinced of it. And they also fall into the category of getting to the point that you offer them a surgical treatment for their fibroids, either myomectomy or hysterectomy. So I think they have to be included in that as well in that same age group. You know, we see patients up to age -- sometimes 44 or 45 who want to preserve their fertility for myomectomy. But we also see women who may be a little older, still premenopausal, but they absolutely do not want a hysterectomy, and you might consider a myomectomy in them as well. So I think you have to include that.

DR. DIAMOND: Okay. Dr. Yustein, have we addressed your question?

DR. YUSTEIN: Dr. Corrado is going to try to pin this down a

little bit here.

DR. CAREY-CORRADO: Hi, Julia Corrado. So the FDA reviewers are taking notes, and we're really trying to make sure that we understand clearly what the message is. And so I'm understanding from Dr. Isaacson that he is saying that that patient in her late 30s, early 40s who wishes to retain her fertility and for whom he has recommended a myomectomy, that with informed consent, he would perform a laparoscopic power morcellation on that patient. I just -- I'm not sure if I heard it correctly, and I want to make sure. And I would have the same question for Dr. Brown. I want to make sure that we understand that the patient in her mid-40s who for some reason maybe not related to fertility wants to retain her uterus and who has symptomatic fibroids, is it your opinion that the benefits of a laparoscopic power morcellation would outweigh the risk for those patients? So that's what we're trying to make sure we understand.

DR. ISAACSON: So my patient is a little bit different because it's one thing if I just want to keep the uterus for whatever reason. It's another issue if you're trying to spare their fertility's potential, which is another factor. And so, you know, I think it changes the risk/benefit profile in my mind if there's a 47-year-old person who says I just want to keep my uterus. And I certainly would suggest an open incision to remove that fibroid with no morcellation whatsoever. However, if it's a 39-year-old who really wants a family in whom the benefits of the laparoscopic or minimally invasive

approach with a small incision, there are fertility benefits that are well documented there. That's where it shifts the risk/benefit ratio potentially on the other side.

DR. CAREY-CORRADO: Okay.

DR. ISAACSON: So I think they're two different scenarios.

DR. CAREY-CORRADO: Okay. Thank you.

DR. CAROL BROWN: So on the other end of the spectrum, you know, I'm an oncologist. I do do myomectomies. I do. But, you know, am I going to morcellate a 45-year-old or a 42-year-old who wants to preserve her fertility? No, I'm not going to because, again, you know, my -- I can't -- to me, a 44- or 45-year-old who wants to preserve her fertility, in my personal hands, I feel that I am going to give her a better oncologic and fertility approach from me by doing it open if it's a big fibroid. That's just my opinion --

(Applause.)

DR. CAROL BROWN: And I'm saying that based on not, you know, that's my technology, my technique. But there are certainly surgeons who all they do is myomectomy, and they may feel -- and as Dr. Isaacson is probably one of those people that, you know, that is somebody they would do it in.

But I think it's, you know, again, just to take a minute here, you know, we're talking about the treatment of fibroids. I think we have to

understand -- and again, for me, it's kind of easy because, you know, unless you are absolutely certain you have to keep your uterus for the purpose of fertility, you know, I think there are other options for treating your fibroids when you're perimenopausal or whatever that don't involve invasive surgery at all, and some of which we've heard about, that I would steer a patient towards rather than any type of surgery. And I think that's something to keep in mind as well. You know, when the indication is wanting to have children or you feel that removing that fibroid is really going to solve the problem, but there are other ways without surgery, without going, you know, that we've heard about such as uterine artery embolization, the focused ultrasound, et cetera, et cetera, birth control pills, IUDs, et cetera, that can be used and should be used -- again, this is our teaching our trainees and reminding everyone there is a whole set of things that you go through before you get to invasive surgery to treat fibroids. And we shouldn't lose that in this discussion.

DR. DIAMOND: Dr. Gallagher?

DR. GALLAGHER: Thank you. This is Colleen Gallagher. I think to your question as you raised it in terms of a woman basically in that age range, for any reason, who might want to keep her uterus, it's important to recognize that some women for religious or cultural reasons feel that their body needs to remain as whole as possible. And so they might be willing to have fibroids removed even with this great risk so that they would maintain

their uterus. So while I'm not saying that it's the perfect solution, I think that if power morcellation or morcellation of any kind remains on the table as an option -- I know we're going to get to the box warnings kind of questions and those kind of things in a minute, but I think some really severe warnings about what that might mean for them would have to be included. Thank you.

DR. DIAMOND: Okay. Dr. Corrado, does that address your question?

DR. CAREY-CORRADO: Yes, thank you.

DR. DIAMOND: Okay. All right. Then -- oh, Dr. Snyder?

DR. SNYDER: I mean, there's enumerable beneficial things, I mean, that have come from, you know, all of this awareness. And we talked about patient education, but -- I mean physician education is going to come through this without a doubt. But I just, I want to just add to what Dr. Brown was saying, even when you're making a decision to do medical management, you know, on a patient, it still requires sound judgment on all of these other risk factors and characteristics that we've talked about.

DR. DIAMOND: Okay. I think we'll now have Elaine Blyskun read us Question No. 6, please?

MS. BLYSKUN: This is Elaine Blyskun.

With respect to device labeling for gynecologic power laparoscopic morcellators:

a. Please provide labeling recommendations for addressing

the risk of an unsuspected malignancy in women undergoing laparoscopic morcellation and for disseminating unsuspected malignant tissue. In your discussion, please specifically comment on whether a boxed warning is warranted and, if so, the crucial elements it should include.

b. Please discuss the information which should be included in the labeling regarding the use of the device in patients with known or suspected malignancy.

c. Please discuss surgical techniques, if any, that may be incorporated into the instructions for use to contain tissue fragment dissemination and enhance the safe and effective use of these devices.

d. Please provide labeling recommendations for addressing dissemination of benign tissue (for example, endometrial tissue or parasitic myomas).

e. Please discuss any other labeling recommendations that are necessary to address the risks on the use of laparoscopic power morcellators for gynecologic laparoscopic surgeries.

DR. TALAMINI: Dr. Diamond, can I ask a quick clarification question of the FDA?

DR. DIAMOND: Sure.

DR. TALAMINI: Can you perhaps give a couple examples of other black box warnings to give us perspective and a framework --

DR. CAROL BROWN: On a device --

DR. HILLARD: For devices.

DR. CAROL BROWN: Not a drug.

DR. MOORE: Yeah. Also, are there any types of warnings that you could give other than a black box warning?

DR. DIAMOND: All right. So the question to the FDA --

DR. CAROL BROWN: What does that mean?

DR. YUSTEIN: So we'll pull up the black box warning example for a device. Drugs uses it much more frequently than we do, but we just had one just recently, so let me pull that up.

DR. DIAMOND: All right. And the other question, I guess, was are there other types of warning that the FDA utilizes other than black box warnings?

DR. YUSTEIN: Are there other things you can address while we're looking that up? I don't want to hold --

DR. DIAMOND: Other than black box warnings, are there other mechanisms that the FDA has to provide warning or information to physicians and/or patients?

DR. CAROL BROWN: I could go ahead and answer one of these

that says -- I think it's (e). Let's see. No, let's see. I'm sorry.

DR. DIAMOND: Sorry, Dr. Brown. I don't know where you are --

DR. CAROL BROWN: Oh, (b), Question 6b, please discuss the information which should be included in the labeling regarding the use of the device in patients with known or suspected malignancy.

DR. DIAMOND: Yeah, okay. Why don't we do that one, and then we can come back to the others. I think that one's straightforward.

DR. CAROL BROWN: Oh, that's what I thought he said to do that while he was looking it up --

DR. DIAMOND: Oh.

DR. CAROL BROWN: Was there anything that we could handle. And so I was just going to take care of that one. You know, I honestly haven't -- I haven't looked at the labeling currently, but if it doesn't say that on the box, it should say that, that this is contraindicated in the use of known or suspected malignancy.

DR. DIAMOND: Okay.

Ms. Aronson?

MS. ARONSON: Yeah. I have a questioning about the labeling on devices. You know, if you have a medication and you go the pharmacy and you get it, and you get your black box warning, a consumer or patient can read that. But with a labeling on a device that's used only by the physician,

how is the patient getting information about the possible risks? And so there does seem to be a disconnect on whether a physician may -- through, you know, whatever reason think that there is low risk and, you know, say don't worry, but then the patient not fully getting this information. So I guess I'm confused about how the patient gets that information.

DR. DIAMOND: I think that's probably the case with any kind of device-related product which is not something that's actually given to or handled by the patient themselves. Let's see. I think Mr. Gardner --

DR. GARDNER: Yeah, Jim Gardner. Along those lines, I think it might help this Panel's discussion if the FDA define what they meant by labeling, because in devices, it's much broader than just the product label. It also includes the instructions for use and any other literature that involves the device and how it's used and what it's used for. So I think that could be helpful if we got an actual definition of that.

DR. DIAMOND: All right. Dr. Talamini?

DR. TALAMINI: So as a starting point, it seems to me that the labeling, a potential labeling might be something like "Power morcellators have been associated with the dissemination and upstaging of cancer in patients with unsuspected tumors during pelvic surgery." Just proffer that. Now, I'm not saying that I'm -- I'm not making any recommendations about whether they stay on or off the market, but if they were to be on the market, I would proffer that as a potential statement or something like it.

DR. DIAMOND: Okay. So you're back at 6a.

DR. TALAMINI: Yes.

DR. DIAMOND: All right. Probably need to do one or the other or we'll confuse ourselves.

Dr. Yustein, you're still looking for the black box warning example, it looks like?

DR. YUSTEIN: I have one example here. It's an in vitro diagnostic test actually.

DR. DIAMOND: Okay.

DR. YUSTEIN: And it's a black box warning that -- and this is, again, for a specific test, and then the test name, "It should not be used without an independent clinical radiological evaluation and is not intended to be a screening test or to determine whether a patient should proceed to surgery. Incorrect use of the test carries the risk of unnecessary testing, surgery and/or delayed diagnosis."

It may be hard to relate that one to this example, but --

DR. DIAMOND: Sure.

DR. YUSTEIN: -- you know, a boxed warning is our strongest level of a warning, you know, a very prominent warning that should be taken into consideration for any use of the device.

DR. CAROL BROWN: So, in that example, who sees that? The hospital that's purchased -- the lab that's doing the test? Like, who would

see that warning?

DR. YUSTEIN: Well, so that gets into the device labeling, you know, as I think it was Ms. Aronson was saying that. So, yeah, so it's in the device labeling, which is, you know, just like any -- you know, it's the package insert that comes with it. Certainly, not all devices are seen by the patient, so it would be the physician or whoever is the end user of that product.

DR. DIAMOND: All right. So why don't we go back to 6b, and then we'll go to 6a after that if that's all right.

So comments on 6b?

Dr. Shriver?

DR. SHRIVER: Craig Shriver. Well, that whole discussion is what is the weakness of the box warning is we think the physician is accepting the risk, but they're not. It's the patients who's accepting the risk. So I don't think there's any good answer to this question because I think it's inappropriate. And, again, only not using the device on the market is the solution.

DR. DIAMOND: All right. So, Dr. Brown, I think your response to this, 6b, was that with a known or suspected malignancy, the device should not be used; is that correct?

DR. CAROL BROWN: Yes.

DR. DIAMOND: All right. Is there anyone on the Panel that disagrees with that thought?

(No response.)

DR. DIAMOND: Okay. So then we would think that the labeling is not relevant because we don't think it should be used in that situation is what I hear.

Dr. Afifi?

DR. AFIFI: I'm wondering if there is a way to use the labeling as a way for the treating physician to inform the patient of the risks. Is that an appropriate thing to discuss in the context of labeling?

DR. DIAMOND: Well, I --

DR. AFIFI: In other words, should the labeling say something to the doctor to say to the patient that if we use the morcellator and if there is a malignant tumor in there that will be morcellated, there's a chance you will lose years of life.

DR. DIAMOND: Yes. I'm not aware that black box warnings have traditionally included messages to care providers to provide to patients, but I'll defer to FDA.

DR. YUSTEIN: Let me get details on that. Sorry.

DR. DIAMOND: Yeah, but we're going to get confused because we're doing too many things at once, so --

DR. YUSTEIN: Sorry. I just want to read this to make sure I understand. Okay. So this is actually for a PMA product, and there is something in the approval order where we inform the company -- and I'll read

it -- "As part of your informal decision process, you must distribute your approved acceptance of risk and informed decision agreement, which will serve as a collective source of information, including patient labeling for the patient. Both the physician and the patient are intended to sign designated sections in order to best assure that a patient has obtained the labeling in an adequate enough time prior to surgery to read it and has understood the risks and other information associated with the device."

DR. DIAMOND: Okay. And that was part of a black box warning or that was part of --

DR. YUSTEIN: No, it's not. It's not a black --

DR. DIAMOND: It's not part of a black box warning?

DR. YUSTEIN: Right.

DR. DIAMOND: Okay.

DR. YUSTEIN: It was a special control.

DR. DIAMOND: All right. So --

DR. IGLESIA: That's special controls? That's a special control mechanism?

DR. YUSTEIN: Correct.

DR. IGLESIA: Physician and patient labeling. And that's different from a black box labeling?

DR. DIAMOND: Yes.

DR. IGLESIA: Okay. Well, that makes sense --

DR. DIAMOND: All right. So we're going to go back to 6a, which I think is where Dr. Afifi has brought us, and now with that in mind, Dr. Simon?

DR. SIMON: Yeah. This gets to the issue -- I'll say more strongly -- that perhaps we're asking the FDA to weigh into the informed consent process, because as Ms. Aronson points out, the black box warning is not something that the consumer necessarily has access to. And so there needs to be some sort of mechanism for a pass-through that we ensure that the information is truly transmitted to the consumer, to the patient, and they're able to understand or at least receive that information. Whether they choose to act on it is another issue but certainly to verify that they have been informed that this black box warning is indeed in place.

DR. DIAMOND: Okay. Dr. Gallagher?

DR. GALLAGHER: Yeah. I think, ethically, we certainly expect that a patient be presented with the risks and benefits of a surgical procedure. And if a particular method is going to be used for that procedure, they should be made aware of those things as well. The only way that can happen is if the physician who is making the recommendation to go to surgery or the surgeon themselves actually do that during the process.

It's usually not something that's put into the document that people sign necessarily like it is in a research protocol, but it needs to be part of the process. So similar to what Dr. Yustein just read, I think, you know,

that kind of thing directing physicians to inform the patient as part of the process is essential, whether that be done both through the black box and another form, in other labeling as a special control.

DR. DIAMOND: Ms. Mattivi?

MS. MATTIVI: So two things. One is with the black box warning, to ask the physicians at the table, does the physician even see that, or you know is the physician the one opening the box and taking out the insert and looking at the indications for use and the labeling?

DR. TALAMINI: This is Talamini. I can partially answer that question. If there is a product with a black box warning, any medical center is going to make that information clearly known to its practitioners if they're even going to allow their practitioners to access it. I think it's --

MS. MATTIVI: Would it be something that the physician sees every time they're going to use this device, or they're going to be made aware of it six months ago, and then not really think about it?

DR. TALAMINI: Yeah. This is Talamini again. I don't think I can answer that question. I just know that the power of the black box warning usually is disseminated to the medical community through multiple channels in powerful ways. And it seems to me, the other physicians can speak, it's usually most powerfully distributed through hospital administrations.

MS. MATTIVI: And then my second comment, again, is just around the informed consent process. Certainly, all the physicians around

this table are very ethical and go through that process with their clients thoroughly. But I think that is also something that we know in the general practice of medicine is not always accomplished as thoroughly as it should be.

DR. DIAMOND: Dr. Mattrey?

DR. MATTREY: Yeah. I was going to second what Dr. Talamini said. When there is a black box warning, everybody knows about it. Whether on the drug side or the device side, when you go to write an IRB protocol or whatever it is, the black box warning comes up all the time. So it's difficult to avoid. Whether it trickles down to the consumer, I don't know, but I think the medical community is aware of every black box that relates to their world.

DR. DIAMOND: All right. So going specifically to this question, then, do we think for an unsuspected malignancy in women undergoing laparoscopic morcellation and dissection that a black box warning would be -- should be necessary, should be a crucial element to include?

Dr. Isaacson?

DR. ISAACSON: Again, I'm not familiar with the black box and the effect of the black box, what it would have. But not to skirt the question, but you had brought up this special control, I guess, that does mandate a signed consent between the consumer -- between the patient and the physician, to me, that would be a much more effective label. I'm fine if you do the black box, too, but as far as its efficacy on making the patients aware

of the risk as well as the physicians, I would say that that would be more effective.

DR. DIAMOND: Okay. And Dr. Brown?

DR. CAROL BROWN: Yeah. I would just ask the FDA if going back in time there is any precedent for this. I have a vague memory that when women first got IUDs, even though it was a drug, you had to give the woman something that she had to sign or had -- you had to document that you had handed her information that talked about the risks. And have there been any other things like breast implants or anything, you know, going back when they first came out, that there was so much concern that the FDA did something to ensure that the consumer actually got directly from the FDA or from the manufacturer the information about the warning, like in the form of a handout or a pamphlet or something that's included in the packaging that you --

DR. YUSTEIN: If Christy Foreman, who is the Director of our Office of Device Evaluation can answer that question, she's much more familiar than I am.

DR. DIAMOND: Okay. Thank you.

MS. FOREMAN: Hi, Christy Foreman, Director of the Office of Device Evaluation. This is not something that we do often in devices. We have a couple examples where we have very specific informed consent documents where there are the risks that are identified that the FDA was

particularly concerned about. There is a requirement for the patient to sign that. There's a requirement for the physician to sign that, that the risk was explained to the patient, the patient acknowledges the risks and accepts the risk. Two PMAs where we've done that have been breast implants and the implantable miniature telescope.

Now, we had a panel meeting a few years back for a product that we had not finalized to regulation, but we had a long discussion about a similar concept that we would implement for special controls. And that was for ECT, electroconvulsive therapy, where there was a specific risk of short-term memory loss. So we had talked about a special control being a informed consent document that the patient would sign indicating that that is a risk and they accept that risk, or their proxy.

DR. DIAMOND: Dr. Hillard?

DR. HILLARD: Paula Hillard. So are you talking only about devices because the IUD is a device that was regulated under the drugs is my recollection, and it did have a specific consent form, patient and physician?

MS. FOREMAN: Yes. The three examples I gave you are three very recent examples that we have promulgated --

DR. HILLARD: Breast implants, IUDs, okay --

MS. FOREMAN: The breast implants, implantable miniature telescope, which is actually an eye implant where there is some potential for cell loss in the eye. So it's a -- basically, a implant for the eye.

DR. HILLARD: But the one that would be much more familiar to gynecologists would be an intrauterine device?

MS. FOREMAN: Yes.

DR. HILLARD: Which, again, correct me if I'm wrong, but that device, that intrauterine device is not regulated by the device, the devices of the FDA --

DR. YUSTEIN: That's correct. That's the drugs end --

MS. FOREMAN: That's correct.

DR. HILLARD: It's regulated as a drug?

MS. FOREMAN: Correct.

DR. HILLARD: And there was a consent form for patient and physician to sign at one point?

MS. FOREMAN: I do believe that is correct.

DR. HILLARD: Yes.

MS. FOREMAN: But there are different authorities under device law and drug law.

DR. HILLARD: Right, right.

MS. FOREMAN: So the three examples I gave you, the two PMAs and the one conversation that we had at a panel meeting were three possibilities under device provisions.

DR. HILLARD: Thank you.

DR. DIAMOND: Dr. Iglesia?

DR. IGLESIA: So I'm still a little bit confused. The breast implant, that had both a black box warning as well as special controls?

MS. FOREMAN: No.

DR. IGLESIA: Or physician and patient labeling or just the physician/patient labeling?

MS. FOREMAN: The breast implants had the informed consent document, no black box warning. The implantable miniature telescope did not have a black box warning. It only had the consent form. The device that Dr. Yustein read, the language from the C.F.R., was a diagnostic test that has a black box warning that we promulgated under Section 520 of the Food, Drug & Cosmetic Act. We promulgated a black box warning for that. It's a restriction. Similarly to that, sun lamps also have a restriction associated with them and a required warning that's similar to a black box warning but not quite.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: So I have to ask a stupid question. Can you please explain in less than eighth grade language what is your usual reason for doing a black box warning? Like, what level of concern? And what does the black box warning do exactly? Who does it reach? What's the intent of it?

MS. FOREMAN: So a black box warning is something that is specifically in the drug regulations. We can accomplish a similar approach.

We have done that in -- as we mentioned one in vitro diagnostic test. That is a threshold that would be our highest warning. So we have a criteria for what is a precaution, what is a warning, what is a contraindication. So a precaution is something people should be aware of. A warning has a higher level of risk. A contraindication is a condition where we actually have information that harm could come to the patient if it's used in that particular manner. And then a black box warning would be a higher level than a contraindication, that it is a very significant safety concern.

DR. DIAMOND: Okay. Dr. Fisher?

DR. FISHER: Just for clarification, you know, I think that you can see that we don't have a whole lot of examples where we've used this in devices. And that's okay, because, you know, I'm familiar with their use somewhat in the drug world.

So I think that what we're trying to say here is that there are a variety of different warnings that we can put on labeling, okay? It can be a precaution, it could be a warning, it could be a contraindication. Sometimes there's actually special labeling requirements that we have that we use under something other than that. A black box warning is going to go at the top of the labeling insert.

So Dr. Talamini actually proposed some wording, and thank you for that. So the idea is that what we're asking is that, you know, do we think that there's risks that are high enough that if we were to still use these

devices, do you think that it would be appropriate to go to the highest level and make sure, regardless of if it goes to the patient or if it goes to the physician, that we were to go with a black box warning. I mean, that's the top of our arsenal when it comes to labeling. That's kind of the question. Maybe you feel that it's not. Maybe you feel that it is. You know, we're not really -- yes, Dr. Brown?

DR. CAROL BROWN: So that's what I was getting at because I didn't -- and I tried to pay close attention in my retraining, but I don't feel like I have enough information about the history, what other things have had black box versus what haven't. I can say that I think that we have a consensus, and again, this is not -- we're not voting. You're just asking us questions and we're answering them. I mean, I would just answer this whole question to say that there should be some labeling or special -- whatever you called it -- controls so that the women who this device is going to be used in and the physicians who are going to use the device both get the message that we do believe there is an increased risk for, you know, whatever -- the wording that you said, as well as that it is contraindicated to be used in known or suspected malignancy and whatever else.

So I do think -- I don't know that we have the expertise -- I certainly don't -- to tell you how you do that, but I definitely would put in a word that there be some mechanism that the patients -- because we heard a recurring theme: No one told me the morcellator was going to be used. I

didn't know about the risk. If I had known about the risk, I would have chosen something different. And I think if there is a way that the FDA can help make sure the women get that information -- and since it's a device and they're not going to the pharmacy to get it and they see it on a label, I think the only way to do that is what you mentioned, like what they did with breast implants and IUDs, in some fashion.

DR. DIAMOND: Ms. Mattivi?

MS. MATTIVI: I think if, as Dr. Talamini said, that a black box warning would help institutions make the decision whether or not to even allow the device to be used in that institution. If that black box warning would assist in that decision, I think a black box warning would be warranted.

DR. DIAMOND: Okay. Dr. Gallagher?

DR. GALLAGHER: I think that I would look for a combination if these devices remain in this kind of use. One would be the black box with what Dr. Talamini said. But I would add to that black box that it has been found that instances of the spread of unknown sarcoma or disease happens, something like that. So you just need something stronger than what we know this way; we also have to say what has happened otherwise.

In addition to that, I would hopefully like to see an informed consent process and document that has to be signed by the patient so that a doctor or someone appointed by them actually can have that conversation and the patient is made aware. And I think that we've heard in a previous

question some things that might actually be listed as contraindications.

Thank you.

DR. DIAMOND: Okay. Dr. Hillard?

DR. HILLARD: So I would just echo the previous comments. I don't think a black box alone would be sufficient. I have no confidence that that would actually get to the patient, so I would completely agree that a black box warning, in addition, a document that the patient and physician would sign as a special control.

DR. DIAMOND: Okay. Dr. Wentzensen and then Dr. Talamini?

DR. WENTZENSEN: I have a practical question to the surgeons. I mean, in many cases, you don't know if you're going to use the device, or do you think that would be a wide range of consenting people for that because you don't know if you're going to use it? So I mean, that's -- which could dilute kind of the -- because you probably won't use it, but just sign it in case. So I'm just asking practically how this would work?

DR. ISAACSON: Keith Isaacson. The example that I would give is we frequently use something called a KTP laser. And each time we use the laser, it requires a consent. So I do have the patients sign that as if we're going to use it whether or not we find disease in which it's necessary. And I would think this would be the same way. Every patient in whom it's even a possibility would have to sign the consent though it may not be utilized.

DR. DIAMOND: Dr. Talamini and then Dr. Snyder?

DR. TALAMINI: So, again, not that we could come up with verbiage or wordsmith, what I have down here is "Power morcellators have been associated with the dissemination and upstaging of cancer in patients with unsuspected malignancy during pelvic surgery. The use of power morcellators is contraindicated in known malignancies." So I don't know if that gets at it, but depending on whether a black box, special controls, whatever, I think that gets near to where we're trying to get.

DR. DIAMOND: Okay. Dr. Snyder?

DR. SNYDER: Dr. Snyder. I also agree that the dual approach is the only thing that will, you know, help me leave here feeling comfortable, because even with your example with KTP, you know, that's institutional-dependent. And what we're, you know, suggesting, you know, makes it universal.

DR. DIAMOND: Okay. Ms. Aronson?

MS. ARONSON: This is a question of the FDA. I'm wondering if there's ever been precedent -- I know that CDC has done something like this, but where there could be dual labeling in a packet that there is the labeling for the physician, but there's also an educational brochure that has the labeling that needs to be presented to the patient, and that sort of -- you know, it's not necessarily consent. There'd be consent also, I suppose, but an educational brochure that --

DR. YUSTEIN: Yeah, we have many products, a lot of PMAs and

HDEs where there is a separate patient labeling or patient document that goes through the device, the surgery, the risks/benefits of the device.

MS. ARONSON: And how does that get in the hands of the patient?

DR. YUSTEIN: I believe that, you know, it's at the doctor's office or wherever the end procedure is being performed.

DR. DIAMOND: Okay. Dr. Brown and then Mr. Gardner.

DR. CAROL BROWN: Two points. One is that, logistically, again, if this, the mechanism of doing that is it's in -- if their manufacturer has to put this in the packaging, the problem that you brought up is that the packaging is going to be open sterilely in the operating room. The patient will be asleep. So you would have to figure out some way to do something with the consenting, et cetera, that would have to be an if, but I think that would be a benefit because then it would make the surgeons think more carefully ahead of time about who they're going to use it in, and then you should be sure, just like I'm pretty sure when I'm going to use a robot, I consent the patient, I tell them all about the risks of using robot and all that kind of stuff, and I have them consent for it. So I think that would be a benefit because it would force everybody to think about it ahead of time.

My only question is, again, not to try to stir up more trouble, but again, you know, this meeting was very expensive, it took a lot of everybody's time. Do we want to limit the comment to pelvic malignancy? I

mean, because again, I don't know, even though I'm at a cancer center, nobody at my place, I think, is using the morcellator deliberately in cancer, but do we need to cover all the bases here since we're going to go to the trouble and recommending to the government to spend a lot of money and do a lot? Shouldn't we include in this anything that we think -- and not just say pelvic? You know what I'm saying? I'm just concerned that, you know, we might be missing an opportunity.

DR. DIAMOND: Okay. All right.

DR. YUSTEIN: Are you talking about expanding into, like, urology and other areas?

DR. CAROL BROWN: Well, Dr. Talamini, I don't know if you could just read again your specific language? Maybe I could address this --

DR. TALAMINI: Yeah. So what I had was power morcellator -- and again, I'm not coming down on whether they should be on the market or not, but if they're on the market, "Power morcellators have been associated with the dissemination and upstaging of cancer in patients with unsuspected malignancy during pelvic surgery. The use of power morcellators is contraindicated in known malignancies."

DR. CAROL BROWN: Thank you. That addresses my concern.

DR. DIAMOND: Mr. Gardner? Oh, I'm sorry. Dr. Fisher, did you want to say something?

DR. FISHER: No. Dr. Talamini clarified that. Thank you.

DR. DIAMOND: All right. Mr. Gardner?

DR. GARDNER: Yeah, Jim Gardner. So, actually, I have somewhat similar questions to Dr. Brown. One was in this dual consent scenario. Where does the responsibility lie for making sure those forms do get signed? Is it with the manufacturer? Is it with the physician? Is it a combination of the two? Just logistically understanding how that works so that it's done right if we go down that path.

And my other comment was about the black box warning as well, though it was a bit on the opposite. We've been talking about leiomyosarcoma, but the warning or the verbiage you suggest was for all pelvic cancers. And I didn't know if that was overly broad or too broad given the subject of this Panel meeting. I just want to throw that out there.

DR. TALAMINI: So this is Talamini. You know, I think it probably would be tough for us here to wordsmith the exact right phrase. I think, you know, getting some concepts is probably the most important.

DR. DIAMOND: Yeah.

Did you want to --

MS. FOREMAN: So judging by Ron's look, I think he wanted the FDA perspective on that. That actually was a large segment of conversation at the panel meeting that I had referenced where we had discussed that, where the practicality of implementing that, the responsibility of getting the signature is on the physician. The manufacturer is not present. So it is a

document that is handed out with each use of the product or each -- depending on how the device is packaged, whether it was an individual package or if it's capital equipment, then it has to be done in form form, or several forms have to be sent with each device. But the responsibility does fall on the physician to explain that, the risk to the patient. And then the physician and the patient are required to sign that. But it is a administrative issue in terms of responsibility.

DR. DIAMOND: Okay. We had questions over here. Dr. Neuman?

DR. NEUMAN: This is a bit outside of my field, but having been a patient and having been given a form usually by some clerk or medical assistant, not the physician, and say this allows us to do this, sign here, I'm concerned that perhaps the patient isn't going to get the information that they need to get.

Similarly, even though I don't have it out on the table here, I have a computer. And when I download software or take it from a disk or whatever you do to put software on your computer, I have all these things that you have to do and indicate that I have read and approve this. Is there some way that this sort of thing can be done and can be mandated by the FDA or whomever to get a better chance that the patient not only sees the material but, in fact, understands it?

DR. DIAMOND: Yeah. Let's see. Dr. Afifi, did you have

something?

DR. AFIFI: Yes. My thought about the informational session where the patient is informed about these risks, it should be for any situation where the morcellation is potentially going to be used, not just for suspected or confirmed malignant tumors.

DR. DIAMOND: Sure.

Dr. Isaacson?

DR. ISAACSON: Mine was just a little bit of the wordsmithing of what you had, even though it's not the right time for it. If you read it back, it says the laparoscopic power morcellator has been associated with the spread of disease. I think I would try to change that as morcellation has been because I don't know that we've seen data that the power morcellator is any worse or any more safe or whatever than morcellation in general. And to understand that the power morcellator is just a tool which is provided to accomplish that.

DR. TALAMINI: So this is Talamini again. I just had the phrase power morcellators, and the only reason I did that is because that's really the only thing the FDA can put a black label box on. They can't on a, you know, ring clamp or something else that somebody may use to morcellate tissue.

DR. ISAACSON: Right. You can put the same label on it even if it says morcellation because that's --

DR. DIAMOND: I think FDA has heard that comment, and we'll

let them figure out how they need to do that from a regulatory point of view.

Dr. Simon, you had a comment?

DR. SIMON: Yeah. Again, not to wordsmith -- I do like Dr. Talamini's black box warning -- I actually would add, you know, to sort of try to close every gap out there the following terminology, "This information should be shared with the patient," so it's actually very clear within the black box warning that there's an expectation that this information is conveyed to the patient.

The last thing I would say is just to recalibrate some thinking, some of these procedures are done in ambulatory surgery centers that are completely disconnected from a hospital. And so while the academic medical centers have very fine processes in place to ensure that information is communicated and there's well-structured committees, in some of these ASCs which are now operating really independently, there aren't the committees and mechanisms in place sometimes to ensure that the black box warning or some of the safety information is clearly conveyed. And Dr. Sobolewski, I think, from Duke sort of touched on some of this just in terms of gathering statistics like this, there's a whole parallel world of care that exists outside of hospitals that is -- we just need to sort of acknowledge and think -- I mean, I think a black box warning gets the physician's attention, you know, when you guys issue one.

DR. DIAMOND: So we're going to go with the presentation --

MS. FOREMAN: Hi, this is Christy Foreman again --

DR. DIAMOND: Thank you. Then we'll come back to Dr. Brown.

MS. FOREMAN: Just to answer your questions, if we were to go the black box warning route or if we were to go the informed consent route, FDA would work out standardized language with the manufacturers, that we wouldn't expect the physicians to have to work on standardized language. We would come up with language that we would consider acceptable and understandable, whether it's communicating to the physician environment or the patient environment.

So this is an example. This is the one document I was referencing for the implantable miniature telescope, which is -- the instructions are to the eye surgeon: "Please review this agreement carefully with your patient for each item. Initial if you are satisfied that the patient understands the item and has accepted it. Your signature confirms that the patient has completed and signed the agreement."

So you can see that the elements are written in plain language so that the patient can understand. "I used an external telescope to see if my vision would improve with magnification. It did. I find the vision acceptable." The patient signs that. The physician signs that they believe the patient understood what benefit they would get from this product.

So this is the type of language we would consider if we went forward for this route. A black box warning would be a black box with very

specific language that would be required of all manufacturers. If that were to be communicated in the labeling and we had to have separate patient labeling, we try and make sure that that wording was such that patients would be able to understand the risk.

DR. DIAMOND: Thank you.

Dr. Brown?

DR. CAROL BROWN: I just want to add some practical experience. So I am old enough that I remember when the implants had to have a thing signed, and I'm at a cancer center. So, actually, the way administratively the cancer center chose to deal with it was they put if a woman wanted to choose that implant, we made a research protocol, an IRB protocol so that every woman had to sign consent and you had to do that. But I'm sure there are literally tens of thousands of plastic surgeons in the United States that could tell you how they did it because they had to -- even if they did it in an ambulatory surgery or their office, they had to document that they had, you know, signed this and their patient had signed it if their patient wanted that certain type of breast implant.

So that is a precedent for, I think -- probably the best precedent for how this would work because it's the same kind of thing. It's something that you only use -- you know, you only open the packaging when you need it and it is done in different settings, and you know, it did -- I think it was effective at getting the message out to the women as well as the

physician. And they didn't -- Dr. Neuman, it didn't become something like what you're saying. It kept it really in the forefront. It didn't become just a routine thing. I know and I think it had the effect of reminding the plastic surgeons, even our plastic surgeons, who, you know, they're not doing this for cosmetic reasons, so they would even tend to more dismiss the purpose of this, it made you really think about it every time you were going to put in one of those implants and really discuss it with the patient.

DR. DIAMOND: Okay. Unless FDA feels otherwise, I think we have addressed 6a. We've already done 6b. I'd like to try to do 6c, d, and e before we break. So if we can change the slide to 6c and give everybody a chance just to reread it? So this is regarding the issue of tissue fragment dissemination and techniques that can be used to minimize that. And I presume this question was meant to include not only malignant but also nonmalignant tissue; is that correct? Yes.

Dr. Talamini?

DR. TALAMINI: This is Talamini. But also this, I mean, the top of the question is with respect to power morcellators, correct?

DR. DIAMOND: Okay. Did any member of the Panel have anything to add from the discussions that we've had so far?

Ms. Aronson?

MS. ARONSON: From the discussions that we've had so far, I mean, I agree with Dr. Shriver that, in some aspect, we're having this

discussion in a vacuum because we're talking about labeling that this technology is going to continue for women with fibroids and with unknown origin or etiology, whatever. So it's like -- it feels like the cart before the horse, because we keep hearing we don't really have all the characteristics. We have a lot, and we're able to, you know, guide some, but it's that one that I'm sitting here thinking about, so I'm struggling with, you know, having this discussion.

DR. DIAMOND: Yeah. And I think we all are. But this is the question that the FDA is asking for us to discuss at this point, specifically, with the use of power morcellation about tissue fragments.

Dr. Brown?

DR. CAROL BROWN: So Carol Brown. So I would answer (c), (d), and (e) that we have not heard -- whereas we heard clear evidence, the best level of evidence as well as MDRs, as well as direct patient accounts of (a) and (b), that there is an increased risk of upstaging and spreading the malignancy and that this should not be done knowingly in known or suspected malignancy, I still think we don't have any information about (c), (d), and (e) to put on a label or anything. And I think that -- so I don't know how we could recommend putting anything on a label about using a bag or this or that when there's no information out there.

DR. DIAMOND: Dr. Talamini, then Dr. Iglesia.

DR. TALAMINI: So this is Talamini. I think that with respect to

surgical instruction and labeling, that's a particularly ineffective -- first of all, I don't think there is an instruction that you could give based on what we've talked about. But, second, I think that's far less likely to have any impact on surgical practice. And I'm trying to think of any examples of any labeling where there are comments about surgical techniques. I think perhaps staplers, but other than that, I can't really think of a good example.

DR. DIAMOND: Dr. Iglesia?

DR. IGLESIA: Yeah, I think that even if you do mention the bag, there is no -- never 100% guarantee that you cannot prevent tissue fragment dissemination with this generation of power morcellators. And, you know, to some degree, I really do respect, you know, industry who are going to be looking at it and hopefully inventing safer devices that don't disseminate. I mean, I think there is technology out there that can suck and morcellate at the same time and minimize that, but you know, I don't think that we can really say anything on a label. And, quite frankly, if you have that label and the patient and the physician are both signing it, you know, I think it's going to bring more of a discussion about what are the alternatives again, Doctor, because it's going to be sort of, yeah, I might want some other options here. And I think that's very important with regards to a true, shared decision-making process.

DR. DIAMOND: Yes.

Dr. Isaacson?

DR. ISAACSON: Yeah. I don't think it ever hurts -- we're not talking about labeling here if I'm reading this correctly. It's more in the instructions for use. And we have several devices, particularly ablation devices, that go through some of the surgical technique in the instructions for use. And I don't think it ever hurts to state the obvious. And I would encourage the manufacturers if they're going to change the instructions for use or modify them to include there needs to be as thorough as possible inspection of the entire pelvic and abdominal cavity that there are no gross tissue fragments at the end of the procedure. And I would encourage the use of copious irrigation if there were -- you know, to suck out the smallest fragments as possible. So, again, there's no harm in doing that. It's obvious surgical techniques, but putting in instructions of use may be helpful.

DR. DIAMOND: Dr. Wentzensen?

DR. CAROL BROWN: They're all on.

DR. DIAMOND: We have microphones that aren't working on the far side here.

DR. WENTZENSEN: Okay. I thought we had seen some evidence for spread of benign disease, so I mean, I would consider adding that to the label as well.

DR. DIAMOND: All right. So I think our answers to 6(c) are --

DR. CAROL BROWN: Sorry. I need to add something.

DR. DIAMOND: I'm sorry. Dr. Brown --

DR. CAROL BROWN: Brown. I have to disagree with Dr. Isaacson. I think that, you know, we're talking about labeling a device, and the things that you said have nothing to do with the device. You talked about, you know, washing out, looking around. That's not the device. That's the surgeon. And I really would, you know, in the interest of future devices and other things, I think you have to limit labeling and warnings about the device as specifically with how you use the device.

So the stapler is a great example because, you know, when you're taking a young trainee through how to use an EEA stapler and do an anastomosis, you will have them pull out that insert and have them read it or have them read it ahead of time so they know how many twists, you know, so that they -- so I think that if there were something that how you use the device itself that might obviate or reduce the risk, then I would say put it in. Like, if you were saying put it in at this angle or do this when you remove it, but I don't think that you can label a device saying you should look around and see if you left anything or you should wash with saline. And we don't know, even though it makes sense, we have no evidence that putting in saline or looking around and picking up all the pieces changes the risk.

DR. DIAMOND: Dr. Simon?

DR. SIMON: I don't want to create a lot of extra work, but it's to Dr. Fisher. When I read these questions, I almost feel like the subtext here is should we be recommending that a bag be used, you know? I mean, when

we've discussed strategies to mitigate risk, really the one thing that was appearing over and over again is, you know, should a bag be used and would that be helpful and would that stop dissemination whether it's benign or malignant? And so I feel like I look at this question, and I mean, are you really asking should we weigh in on something like a bag?

DR. FISHER: You know, I think we pulled from the experience that we have. And we know that containment devices are being used, bags are being used. You know, I've heard -- yesterday I heard that they were used in GYN procedures, but we got away from them. So, you know, I don't know that it's an endorsement that we're pushing you at. I look at it in a bigger context and say not necessarily bags, but containment devices or procedures. So, you know, I think that when these were put together, you know, I was looking at them from my experience, and kind of the default was the bag, but I hope it wouldn't be limited to that.

DR. SIMON: Right. No, I think one of the strengths -- sometimes the FDA is to try to actually encourage innovation and not discourage it. And I would hope that for companies or the corporate world or even engineers or whoever is thinking about this, that the meeting ends with sort of an energy to look at this problem and figure out ways to truly mitigate this risk and solve it. And it's not to see these black box warnings as a squelching of innovation, but actually an encouragement of that, and I just want to make sure the language actually somehow reflects or the behavior

reflects we are continuously looking to improve things and not discourage growth.

DR. DIAMOND: Okay. Let's see.

Dr. Yustein?

DR. YUSTEIN: Sorry, Dr. Diamond. Can I just go back to the discussion between Dr. Brown and Dr. Isaacson? Dr. Isaacson had mentioned what he called "state the obvious things" for some of the surgical techniques. And Dr. Brown, from the regulatory standpoint, there would be nothing that would prevent us from putting items like that in the labeling. We certainly could. If you consider that the fact that the devices cause fragmentation and some of the things that Dr. Isaacson was talking about was meant to address what the device ended up doing, it wouldn't be inappropriate for us to put things like that in the labeling.

DR. CAROL BROWN: I disagree. I think it is appropriate -- it is inappropriate because we do not -- this Committee -- I have never seen any evidence that washing out the cavity after you spill cancer cells does anything. We all do it, but we don't have any evidence that shows that it does. And I think that the FDA should be about evidence and science --

DR. YUSTEIN: Right.

DR. CAROL BROWN: -- and I think anything you put on your label you should have evidence that it's going to do. Because, again, the physician and the woman are going to then think, well, even though I did all

this, if I did have an unsuspected sarcoma and you looked around and washed everything out and got every piece, the implication could be that you're going to be okay. We just don't know that. Once we do know it -- and I do think these things should be tested. I agree. We need innovation. We should do testing of bags. We should do some studies. And once you have the proof that the bag blocks the cancer cells getting across it, then you put that on the label. But I just don't think you should put stuff on the label until you actually have evidence that it worked.

DR. YUSTEIN: So I actually agree with you. What I was doing was talking from a higher level, that we can put things like that in the labeling. If the Panel doesn't agree that those things have evidence to support it in the labeling, then that's a different question.

DR. CAROL BROWN: Okay. So just to be clear -- Brown -- I don't think that we have evidence, you know, to support, although it makes perfect sense that any -- again, I think we're trying to send a message here that we haven't heard evidence that anything -- once you've violated the, you know, the cancer, we don't know what you can do to mitigate the risk. So we don't have those evidence.

DR. DIAMOND: Ms. Mattivi?

MS. MATTIVI: So my cynical side, and maybe this is a question for Mr. Gardner. But, you know, we talk about innovation and the companies being motivated to continue to innovate and improve their products. If their

product remains on the market and in the operating rooms and is being used and is generating income, how much motivation is there really for the companies to continue to look at this? I mean, I give kudos to Ethicon for holding distribution, further distribution of their product, but they're certainly not the only manufacturer of this device. And they didn't pull their devices from operating rooms. They just held on further distribution. And, again, this is my cynical side talking.

DR. DIAMOND: Mr. Gardner, do you want to respond or --

DR. GARDNER: Kris, you were looking at me. Jim Gardner. You were looking as if there was a question. I'm not sure I heard a question. I'd be glad to answer a question if there was one, or I can --

MS. MATTIVI: The question is: Really, in the real world, how much motivation will there be for companies to continue to look at innovation for these devices as long as they remain in use?

DR. GARDNER: Yeah. I certainly can't answer on behalf of every medical device company in the world, and in fact, I don't work for one that makes one of these devices. But I can say, at least the companies I am familiar with that, you know, we work in a very competitive environment, so on a very practical level, we're always looking to improve our products to come up with a better product because that means that we survive as a company. I can tell you my company that I work for, we make a profit so that we can reinvest, so that we can innovate. That's our reason for being, is to

manufacture tools for physicians to use to take care of patients. So I don't think any device company that has survived will continue to survive if they're not continuing to try to improve the products that they manufacture and bring to market.

DR. DIAMOND: Okay. I think we're going to go on to 6d.

Dr. Talamini, go ahead.

DR. TALAMINI: Well, I was just going to make -- this is Talamini. I was just going to make the comment that I think an equally plausible scenario is that if this remains on the market with these sorts of warnings, they may disappear entirely, because I doubt they're a large margin item for most of these device companies. So I think it's equally plausible that with -- if this remains on the market with this set of warnings, it may be very hard to find a power morcellator. So I think either scenario is possible. We really don't know.

DR. DIAMOND: Okay. So 6d talks about now labeling recommendations regarding dissemination of benign tissue, and I think in some ways, we've discussed this in response to some of the other questions, but does anyone have anything specifically to add in regard to -- in addition to what's already been said?

(No response.)

DR. DIAMOND: Seeing none, Dr. Fisher, Dr. Yustein, anything explicit you want to ask about 6d that we haven't addressed?

(No response.)

DR. DIAMOND: And if not, we're going to go on to 6e.

Dr. Isaacson?

DR. ISAACSON: The only one thing, I'm not sure where this came from because I've never seen data that the morcellation of a uterus exposes a patient to a greater risk of endometriosis or something like that, and I'm not sure if that's what you were getting at?

DR. YUSTEIN: No. I think we were talking about dissemination of endometrial tissue, not that it causes endometriosis.

DR. ISAACSON: For cancer, of endometrial cancer?

DR. YUSTEIN: No.

DR. ISAACSON: No?

DR. YUSTEIN: No. So this would be benign --

DR. ISAACSON: Which would be endometriosis?

DR. YUSTEIN: Right.

DR. ISAACSON: And I've never seen data that that's been associated, the two have been associated.

DR. YUSTEIN: That laparoscopic power morcellators have spread endometrial tissue?

DR. ISAACSON: Or any morcellation would.

DR. YUSTEIN: I think we've provided that in the Executive Summary. I think we provided some references with that --

DR. ISAACSON: Creates endometriosis?

DR. YUSTEIN: Um-hum.

DR. ISAACSON: In the peritoneal cavity?

DR. YUSTEIN: Um-hum.

DR. ISAACSON: Not in the abdomen --

DR. DIAMOND: Well, there may be an association between having had a morcellation of endometrium --

DR. YUSTEIN: Right.

DR. DIAMOND: -- and subsequent development of endometriosis, but whether that's cause and effect --

DR. YUSTEIN: Right.

DR. DIAMOND: -- I don't know that -- I don't remember the document, but I don't know how someone would truly have known that.

DR. YUSTEIN: Right, okay. I can try to find the references if you want.

DR. DIAMOND: Yeah. 6d, anybody have comments?

(No response.)

DR. DIAMOND: If not, we'll go to 6e, labeling recommendations regarding risks of use of laparoscopic power -- other labeling recommendations regarding risks of laparoscopic power morcellators from gynecologic laparoscopic surgeries.

Dr. Brown?

DR. CAROL BROWN: So this is Carol Brown. So, again, you know, I really learned through this process that the laparoscopic power morcellators didn't really go through the same kind of PMA thing to begin with. And so my understanding, and I direct this to the FDA, is that in addition to the notifications that you've been getting since December 2013 about the risk of spread of -- intraperitoneal spread of leiomyosarcoma, there also have been MDRs about other things, such as including six deaths that were probably associated with a major visceral or vascular injury. So I would like to -- I have a personal -- I would be concerned that since you have those MDRs as well, to not miss an opportunity and just remind the people that are going to be sticking this thing inside near bowel, bladder, major blood vessels, that it has been reported that people have died from, or however you want to word it, but I would like to see some -- if you're going to do this, I think it would be a missed opportunity not to add some caution about visceral injury at least based on the limited information I saw from those MDRs.

DR. DIAMOND: So visceral and vascular, would that be --

DR. CAROL BROWN: Visceral, yeah, and I guess vascular, visceral and vascular would be -- sure.

DR. DIAMOND: Okay.

Dr. Gallagher?

DR. GALLAGHER: Yes. Earlier we talked about some

contraindications, situations -- I think that those contraindications should also be added to the label.

DR. DIAMOND: Dr. Isaacson?

DR. ISAACSON: This is my opportunity to counter Dr. Brown. I think every single device we used, almost every single device we use in surgery has been associated with some complications and deaths, including and not limited to the endometrial -- all the global endometrial ablation devices have had deaths reporting in the MAUDE database, the tools you use such as harmonic energy, such as laser energy, such as ray of frequency energy, have all been associated with complications that have ended in death. So I don't know that this is, again, another surgical tool that, when used, if it is used inappropriately or improperly can lead to a complication. And I don't know why you would want to single out this tool to be associated with vascular complications or risk of bowel injury when we're not doing that with every other surgical tool.

DR. CAROL BROWN: So this is Brown. If I may answer, again, and maybe this requires another meeting, because, again, I wasn't aware that there had been these reports, and maybe there needs to be -- maybe the FDA or someone else needs to go back and look at those reports. But intuitively, again, as a surgeon, you know, it isn't the same because it's a spinning knife, and you're sticking it in laparoscopically. And, you know, there have been concerns raised about injuries using other minimally invasive new

technologies to vascular injuries and so on.

And, again, I guess what I'm saying is, I wouldn't on its own do that, but if you are going -- if the FDA is going to put a black box warning and labels about the risk of spreading malignancy, just looking at the numbers, and again, I don't know if this is true, maybe you have to go back and look at it, but it just struck me that you had, you know, you have six people who bled to death essentially from what should be completely preventable, because if you're looking at it all the time, and you're, you know -- so, again, I acknowledge what you're saying, but I don't think it's exactly the same as endometrial ablation.

And, you know, and maybe there have been similar reports, and, you know, what is the risk. But if you're going to put a label on about the risk of spreading cancer, I also think just numbers wise, in terms of what's been reported to the FDA, I don't know if there is literature out there about this. I don't think anybody is studying it, but you have those MDRs, and so I just would question don't you have an obligation since you got those reports to either investigate that more or to put some general warning on about it?

DR. DIAMOND: Dr. Iglesia?

DR. IGLESIA: So I don't disagree with you, but I don't know if it's necessarily the role of the FDA since they're not really in the realm of the practice of medicine or training. I think that's really our jobs, you know, as educators, as leaders. New technology. I mean, I always remember this line

from the editor of the *Lancet* that no innovation without evaluation. And that means that surgeons need to have the proper training. And so we have surgical errors maybe because we weren't trained properly. These are new things that weren't even developed when many of us were starting residency. And, currently, like, our residents go through simulations and, you know, we have morcellators that we use hysteroscopically, I mean, on potatoes and all -- we have a special lab, and we have to observe. And we, you know, look at that kind of stuff.

But for those of us in practice who are getting new to this technology, how do we safely introduce it? And I think that's sort of a separate situation outside of what the FDA is doing. And that's what all the societies, ACOG, SGS, AAGL, SGO, I think that's our responsibility.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: So, again, just to clarify. I don't see this as a training issue. Again, you know, I listened to everything, and I can't remember who -- where I saw that data. I think it was Dr. Kobolewski [sic], where he had that slide that said the MDRs about deaths. And I asked about it because, again, it just struck me as a surgeon and having seen these things used and knowing about, you know, during regular laparoscopy or robotic laparoscopy, cutting into the vena cava, et cetera, and knowing what that means, again, the idea of the spinning knife and all of that, it just struck me. So maybe my question is should the FDA also just look into that aspect of it

as well, because it seems to me you might be getting a signal from out there that you haven't heard yet, or maybe we need to get more information just like this signal. And on the surface of it, it just sounds like it's equivalently a concern.

Again, as a surgeon, to me, to have somebody, you know, bleed to death because of this, it's very horrible. So I'm just raising the point. I don't know if the FDA can comment about whether the reports that they've gotten -- or has this really been looked into. Again, this device did not go through the usual process of having to talk about what are -- these devices did not -- my understanding, they did not go through the PMA process to begin with where all of this would have come up. They're not hearing about it later. So since we heard about the leiomyosarcoma risk, I heard, again, I'm not sure if I was right, but I thought I heard that you've got reports in your MDR that six people died from vascular injury. That seems to be a lot to me, but I don't know.

DR. DIAMOND: Okay. That's a message I think the FDA can take back and can look into.

DR. FISHER: Right. Point taken. I think that, you know, yesterday we talked about some of the limitations and, you know, our ability to pull additional information out of that and, you know, point taken.

DR. DIAMOND: Dr. Snyder?

DR. SNYDER: Yeah. I mean, I just -- I agree with Dr. Brown.

You know, we're sitting here dealing with a device, and it -- I mean, one, we can't ignore, you know, additional risks that we're seeing. And, two, I also agree that if you've included, you know, a certain, you know, subset of risks, you know, that it is dangerous to not actually include all of the risks, you know, that we've heard about. And before, I may have felt differently, but from what I've heard today, you know, you know, we're not doing a good job discussing the risks.

DR. DIAMOND: Okay. All right.

Dr. Fisher, Dr. Yustein, other things that you want to hear about Question 6? Otherwise, we're going to take a break.

DR. YUSTEIN: No. But I could share the reference with Dr. Isaacson. It was a case report, and it was a patient who underwent supracervical hysterectomy for fibroids and then was found to have disseminated endometriosis at a later time. I have that case report.

DR. ISAACSON: Excuse me. It was one case report?

DR. YUSTEIN: Yeah, one case report.

DR. ISAACSON: Yeah, okay.

DR. DIAMOND: Okay. So we're going to take a break for 10 minutes, and then we'll resume.

(Off the record.)

(On the record.)

DR. DIAMOND: All right. We're going to go ahead and resume

the Panel meeting again. We are going to go to FDA Question No. 9. And we'll ask Elaine Blyskun to please read the question for us, please.

MS. BLYSKUN: Thank you. Elaine Blyskun. So in this last question, we're going to switch gears a little bit -- hopefully get out of this screen. So we're going to be talking about how we might review future devices. So as I go through this question, I'm going to be providing you with a list of risks to health posed by laparoscopic power morcellators, and then also potential mitigation. So these are things that we would be looking for in future designs that would be subject to all manufacturers. And so it may not apply to the current designs and our current state of device review, but going forward, we're looking for your input.

So Question 9 revised is:

Gynecologic laparoscopic power morcellators are currently regulated as Class II devices. FDA's regulatory decision-making is driven by an understanding of the benefits and risks for a device type. FDA would like the Panel's input on the risks to health posed by laparoscopic power morcellators for gynecologic use and appropriate mitigations to inform FDA's regulatory decision-making for this device type.

The following table includes risks to health and potential mitigations. And so I'll let you read through that.

(Pause.)

MS. BLYSKUN: Dr. Diamond?

DR. DIAMOND: That's the question, yes. We have problems with our microphones again.

DR. WENTZENSEN: Nicolas Wentzensen. I'm trying to understand. This is specific to the Class II regulation or are you asking, like, more general? Are you asking a wider question?

MS. BLYSKUN: Yeah, more generally, more generally. Aside from the regulation, these are the risks that we have identified, and these are the potential mitigations for those risks.

DR. DIAMOND: Yeah. And the question to us will be coming in about three more slides.

MS. BLYSKUN: Yeah. Hang on. Can I advance the slide?

DR. DIAMOND: Go ahead, please.

MS. BLYSKUN: Okay. This is a continuation of the previous table.

(Pause.)

DR. DIAMOND: Okay. And I remind the Panel also, this is what you have in front of you on the handout as well, the specifics, so we can refer back to them.

MS. BLYSKUN: Left side is risks, right side is potential mitigations.

DR. DIAMOND: All right. If you want to go on.

MS. BLYSKUN: Okay. I've had a request to read it so it's in the

transcript.

DR. DIAMOND: Oh, okay.

MS. BLYSKUN: Sorry. Okay. So I'm going to go back.

So on Slide 12, identified risk, dissemination of unsuspected occult cancerous tissue beyond the uterus. The potential mitigation measure for that is non-clinical performance testing/specimen containment system. Also, labeling and also training.

The next identified risk is dissemination of benign tissue, and the corollary potential mitigation measure is non-clinical performance testing/specimen containment system. Also, labeling and also training.

The next identified risk on this slide is injury to non-target tissue. And the related potential mitigations are non-clinical performance testing, labeling and training.

On Slide 13, as I mentioned, the left column denotes the risks that we've identified. The first is inadequate sample to determine pathology. And the potential mitigation is non-clinical performance testing.

The second on this slide is nerve/muscle stimulation, with potential mitigations of labeling and training.

The third is device malfunction leading to injury, with related mitigations of software verification, validation and hazard analysis, non-clinical performance testing, labeling and training.

The last risk on this slide is electromagnetic interference, with

potential mitigations being electromagnetic compatibility, EMC, and electromagnetic immunity, EMI, and labeling.

The last portion of the table is on Slide 14. The first risk identified on this slide is electrical shock, with related potential mitigation being electrical bench testing and labeling.

Next is adverse tissue reaction, with potential mitigation of biocompatibility.

And then last is infection, with potential mitigation of sterilization, cleaning and disinfection, as well as shelf life testing.

Okay. So --

DR. GARDNER: Jim Gardner. I had two questions I was hoping you could answer about this. On the first table, you have nonperformance, performance testing/specimen containment system. Are you suggesting that future morcellators would have a tissue containment system that went along with them or would this be --

MS. BLYSKUN: It's possible. So the way that we're approaching this is to anticipate future design.

DR. GARDNER: Okay. And then my second question is about training. I'm assuming these are mitigation measures taken on by the manufacturers. So is it manufacturer training of users? Are we talking about --

MS. BLYSKUN: I think we mean in the broadest sense possible.

It could be the manufacturer training. It could be other training that's identified as a result of the discussions that perhaps other entities may take up.

DR. GARDNER: Okay. Thank you.

MS. BLYSKUN: So getting to the text. Please comment on whether the above are a complete and accurate list and are adequate to mitigate the risks to health for gynecologic laparoscopic power morcellators. Please comment on whether you disagree with inclusion of any of these mitigations or whether you believe any other mitigations should be considered. In addition, please discuss whether clinical data are necessary to address any of these risks. If so, please identify which risks, the type of clinical data to be considered, and how the clinical data could address the risks.

DR. DIAMOND: Okay. Thank you.

MS. BLYSKUN: Is this slide --

DR. DIAMOND: I would leave this slide on, I think, because everyone has the table in front of them.

So the question I'd like to first ask the Panel members is whether this is a complete and accurate list of the risks and approaches to mitigate them? Dr. Isaacson?

DR. ISAACSON: Keith Isaacson. The only thing, again, going back to -- I think given that there was just one case report of dissemination of

benign tissue, that based on that and the number of cases that have been done, I would eliminate dissemination of benign tissue as an identified risk.

DR. DIAMOND: Okay. Dr. Shriver?

DR. SHRIVER: Shriver. I agree with the list as being complete and adequate. Mitigating the risks, I guess we'll get to this next, Dr. Diamond, but I think these proposed measures are not adequate, and seven of them should be the part of a randomized prospective clinical trial for future devices.

DR. DIAMOND: Dr. Wentzensen?

DR. WENTZENSEN: Yeah, Nicolas Wentzensen. I agree. I don't know how especially the risks on the first slide would be measured with non-clinical data. I just don't understand how that would work.

DR. DIAMOND: Okay. I saw another hand over here.

Dr. Neuman?

DR. NEUMAN: I think the list is complete, although some of the items on the list are of less importance than others. I also think that for most of the items, there already exist bench testing that some of which I believe the FDA mandates for other devices, but certainly, the clinical engineering community does. So, you know, I think in terms of bench or, in some cases, animal testing, these types of things can be done and can be relatively easily be done with existing standards, and I would encourage this to be required for future devices.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: I just had a question. Are all of these risks things that we received information about, because I don't remember reading anything about electrical shock, and I'm not sure what -- I'd like a clarification -- I don't know what adverse tissue reaction means, and I don't know what exactly you mean by electromagnetic interference.

DR. PRICE: Yeah, so these are known risks which have been reported with this device class or known risks associated with, like, an electrically powered device. So we don't have to have reports of electrical shock with a power morcellator to know that that's a real risk, and they need to do testing to show that it's electrically safe.

When we talk about adverse tissue reaction, again, we're trying to do this at a very high level. That's talking about material safety and infection, you know, that you -- if it's a sterile device, that you have provided us information that shows it is sterile.

DR. DIAMOND: Mr. Gardner?

DR. GARDNER: Jim Gardner. We spoke earlier right before the break about possible labeling changes and whether those would stimulate innovation and lead to better devices or perhaps staunch innovation and have manufacturers actually leave the market. And I couldn't give a straight answer to that, but I wanted to make a similar observation. I think the more that's being asked for, the more it will require manufacturers and innovators

to think is this is a market I want to enter into or not. And I'm particularly thinking about if randomized clinical trials are required, I think manufacturers who are interested in developing morcellators are going to look long and hard about what that would entail and what the studies would look like and how large they might need to be and whether it was something even feasible for them to do.

DR. DIAMOND: Ms. Mattivi?

MS. MATTIVI: So I have a question. Are these requirements for all devices currently on the market as well as new devices coming to market or just one or the other?

DR. PRICE: No. As Ms. Blyskun said, this would be moving forward. Now, that's not to say -- most of these are already required of the devices that came through, but you'll see that there -- I mean, the whole purpose of our discussion today about dissemination of unsuspected, that was not a risk that was previously, you know, mitigated with any sort of testing. So this would be for moving forward.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: So when it says -- when you list what are the mitigating measures, I think that we said that we didn't feel confident enough to say that a specimen containment system, i.e., a bag, is going to mitigate the risk of disseminating the occult cancerous tissue. And I would also say the benign tissue. So I'm not sure if that was said before, but I

wouldn't agree to put that as a possible mitigating measure under those two.

DR. DIAMOND: Dr. Simon?

DR. FISHER: Could I --

DR. DIAMOND: Oh, sure.

DR. FISHER: Excuse me. Could I provide some clarification? So we're not looking at necessarily where we are now. I mean, we've had discussions on the bags. And actually, for the discussion, if it says bags, I'd like to change it to containment systems, okay? So, you know, we're looking forward. You know, if we feel that they're inadequate now, what we're asking you to say or what we're asking your input on is, as we move forward, for the innovative people that are out there if they decide to come in with something like this, this is what they would have to show. They would have to show that their containment system was a good containment system. And if they were to come with that, come to us with that, what would they have to show. So that's how we're looking at these.

DR. DIAMOND: Dr. Hillard, then Dr. Iglesia?

DR. HILLARD: Paula Hillard. So my question is if or how the answers to these questions relate to the classification of the device. So does this relate at all to -- do our answers to these questions relate at all to this being classified as a Class II or a Class III device?

DR. FISHER: Well, I think that that's actually what we're looking for. We're looking for information to help us figure out what would

be required, if it's possible, and we're going to take that information back, and that's going to help to lead us for our next step.

DR. HILLARD: So is there an answer that we would give that would say that we would recommend that this be classified as a Class III device?

DR. FISHER: We're not looking for that right now.

DR. HILLARD: You're not looking for the answer to that question?

DR. FISHER: No. We're actually just trying to see if there are risks that we haven't taken into consideration and some of the mitigations that we've put up there, if there's additional mitigations that might be considered. So, no, we're not to the point of that discussion yet.

MS. BLYSKUN: If I may, I think one way to look at it is independent of class. Regardless of the class determination, is the list of risks that we have identified and the potential mitigation sufficient? And then we can take that information and interpret it in terms of what we might do next in terms of next steps with classification.

DR. DIAMOND: All right. So Dr. Iglesia and then Dr. Simon?

DR. IGLESIA: Cheryl Iglesia. So as a general category, as general categories, I think the seven listed are appropriate. And I think that clinical data are necessary with the first four. The caveat is we need a comparator in that I think there's a problem with just morcellation itself,

power or no power, in terms of clinical data, morcellating uteri, you know?

DR. DIAMOND: Dr. Simon?

DR. SIMON: Yeah. I sort of touched on this yesterday a little bit, and maybe I could get Dr. Afifi to comment here. In terms of getting this clinical data or randomized trials, you know, you have a disease with a prevalence of, let's just say it's 1 in 1,000 to make the math easy. So to Dr. Afifi, you know, what does the study look like to detect a signal of improvement if -- you know, how many patients do we have to enroll if we have a very limited interpretation of what this randomized trial should look like? I think we need to then allow the FDA to consider maybe surrogate endpoints in terms of a trial to look at innovation to allow companies to say it can be an animal trial, because I think a trial with people to detect a signal on something like leiomyosarcoma, you know, is -- you know, you can tell me, Dr. Afifi. How many patients are we talking about enrolling?

DR. AFIFI: Off the top of my head, it would be thousands, perhaps tens of thousands, yeah, for something --

DR. SIMON: Which I think is -- I mean, that trial -- I mean, it would just never happen. There are no resources to run that trial. So I think we would need to at least have the FDA think about, yes, we need to have data on these -- on containment systems, but we need to acknowledge that if we want to encourage innovation here, demanding a clinical trial to look at an endpoint is just not feasible if that endpoint is disseminated

leiomyosarcoma. I mean, we'd have to understand that there are other ways to sort of get this information.

DR. FISHER: Right. And I was waiting for that last -- Fisher, FDA -- I was waiting for that last part of your sentence, you know, what was the endpoint, what are you looking at --

DR. SIMON: Well, no, I --

DR. FISHER: Because just to say -- no, no, no, it's valid, you know, but just to say that we're going to do a clinical study, what I'm trying to glean out of this is a clinical study, what are the endpoints that we -- I mean, are we looking at the spread of cancer, are we looking at dissemination of cells?

DR. SIMON: Right. Well, I think if we -- I take a step back and I say, listen, in a perfect world, we would have no financial limitations and we could run every trial, and patient enrollment would be spectacular and, you know, wouldn't that be great. But we don't live in that world. And so I'm just trying to think.

So if I was approaching this problem as someone who wanted to solve it, I would say, okay, I want to come up with a containment system so -- that can really, you know, allow us to get back to the good old days when we could remove a uterus through a tiny little hole. So we need to demonstrate to the FDA that we're going to collect every single cell that possibly comes out of this thing, and not a single cell will end up in the

abdomen. You know, I would have to come up with an animal model that would, in some ways, validate that for you and maybe even, you know, a method of detection of cells that would potentially validate that with you, you know?

So we would need to design an experiment that verifies that, and how that experiment is defined in an animal or a bench system, I don't know. But someone would need to do it, because the alternative is to say let's provide the clinical data. And to Dr. Afifi's point, really, do we think anyone is ever going to be doing, you know, a 10,000-person study to detect this signal? This is one where now, you know, listen, we hope the incidence of LMS is on the order of 1 in 7,000. That would be great. I'm not sure it's there. If you're actually looking for a clinical signal, now we want the LMS to be on the order of 1 in 100, because then at least we can detect an improvement.

DR. FISHER: Point taken.

DR. SIMON: So I don't think to get data, maybe, clinically, it's not there. Maybe someone can come up with a -- I mean, it's like we want someone to -- you know, you want to encourage people to look at biomarkers, to look at DNA, to look at something that gets us there. That's just my point.

DR. FISHER: And I would agree. Actually, we're looking at alternatives. So the first part as we move through these questions, I think

part of it deals with, you know, what can we get out of bench testing, what can we get out of animal models. And I think the last part of the question is do we need clinical data, and if so, what are we trying to answer. So I appreciate your comments. And I agree if you're looking for a very small signal, you're looking at a very large patient population. Get it.

DR. DIAMOND: All right. Dr. Afifi, Dr. Brown, and then Dr. Talamini?

DR. AFIFI: So if the outcome we're looking for is the occurrence of a dissemination of a malignant tumor, let's say 1 in 500, 1 in 1,000, then we need thousands of cases. But if the outcome you're looking for is whether when something exists, will it be disseminated, then that could be a designed experiment, and probably a bench experiment might be the way to go. And then if there's a mitigation method, be it a bag or something else, then you could compare with and without the mitigation, and then it would be quite a manageable such an experiment, because you have put something there to see if it's disseminated or not, okay, with and without the mitigation. That one could be a designed experiment. But it would need to be either a bench -- I don't think animal model would be appropriate there either. I think probably some engineer-designed bench experiment.

DR. DIAMOND: Okay. Dr. Brown?

DR. CAROL BROWN: Carol Brown. So I don't -- I disagree with -- I think for the dissemination of unsuspected occult and dissemination

of benign tissue, you do not need -- I think you could do non-clinical data. I mean, this could be an Intel science project. Design a system that is going to remove particles of a certain micron size without them escaping. I mean, I can sit here and think of ways you could do that. You put something in water and you color the -- you know, there are lots -- that's what you're talking about here, I think. I don't think you have to have the clinical because you're never going to get the clinical endpoints of leiomyosarcoma, benign. Those things are so rare. What you want is a device, a bag, or a morcellator itself that you can put some type of non-clinical system, which you could simulate in a lot of different ways that I can think of off the top of my head, and measure that particles of a certain size don't leak out of that system.

You know, we have certain masks that we must wear when we use a laser and we're vaporizing HPV-containing lesions. And I'm trusting that the FDA or whoever has approved that mask, that those certain microns that will not get through that so that I don't get, you know, head and neck cancer. It's the same kind of principle. I don't think you have to go to the endpoint, because, again, the endpoints are caused by dissemination of cells. So there should be some way to work this out from an engineering standpoint to be able to measure that, and I don't think it would have to be a huge deal, and I would think that this is something that these companies could do pretty quickly, you know, and it would be quite interesting.

DR. DIAMOND: Dr. Talamini?

DR. TALAMINI: Talamini. Does non-clinical performance testing include animal models?

DR. FISHER: Yes, it does.

DR. TALAMINI: Okay. Well, then I agree. I'm imagining people bringing innovative solutions to this, focused ultrasound, sonication, whatever it might be, and I think those would need to be tested in animal models in terms of injury to non-target tissue.

DR. DIAMOND: Dr. Mattrey, did you have a comment?

DR. MATTREY: Yeah. I kind of disagree with the engineering principle. I respect engineers. I was one of them one day a long time ago. You have to mimic the clinical scenario. So you have to have an abdomen. You have to be able to put whatever you want to take care of in a bag. You have to, you know, handle the bag, which can tear, all these things. And I think animal models are possible by using labeled cells, fluorescently labeled cells, or some other tracer that can be placed in a uterus or whatever, and then handled in a clinical-like fashion, or otherwise, you'd have to go to the clinic. And I would discourage doing that because I think that would take a lot of effort; plus, I'm not sure based on the data we've heard today that that's really ethical.

DR. DIAMOND: Okay. Other comments from the Panel?

(No response.)

DR. DIAMOND: Questions from FDA? Dr. Corrado?

DR. CAREY-CORRADO: Hi. I want to follow up just a little bit, because when the meeting convenes, or when it adjourns, we're really going to have to interpret a lot of what has been said here. So there was discussion yesterday and today regarding usability of bags, deploying them, having adequate visualization, being sensitive to tissues that may be on the other side of the bag. And so, therefore, I'm worried about the non-clinical models. The animal model could work, but I want to make sure that the Panel would be -- would find it acceptable to do bench and/or animal as opposed to clinical given what we have heard about the possibility of injuring a tissue, causing a severe vessel injury. That is something that we certainly couldn't evaluate on -- in a bench, you know?

Yes, Dr. Brown?

DR. CAROL BROWN: So, again, then that brings up the issue of Class II, Class III. So there are bags out there that are already approved for use in humans, right? Are those Class II or Class III, meaning -- they're Class II?

DR. CAREY-CORRADO: In general, they're Class II.

DR. CAROL BROWN: Meaning that they haven't gone through the PMA process. So, you know, I guess what we're saying is -- what I'm saying is I think the question of the dissemination of the particles can be most of the work -- I agree with you. You'd have to get to some type of model of a clinical situation, which might involve animals or it might not. I

think you could create a model that isn't an animal where you could test that. But I do think the safety parts of whatever it is, whether it's a new type of morcellator that's completely enclosed or whether it's a bag, would have to be tested in some type of model where those organs are at risk, yeah.

DR. DIAMOND: Ms. Blyskun?

MS. BLYSKUN: This is Elaine Blyskun. Dr. Brown, I have a point of clarification. Could you explain what about the PMA process gives you assurance? You mentioned that, you know, bags did not go through the PMA process. I'd just like to learn a little bit more about what you're looking at in terms of that comment.

DR. CAROL BROWN: Okay. Carol Brown. Sorry. I'm probably misunderstanding this. So just simply through this whole process, what it seems to me part of the problem with the laparoscopic power morcellators were that they were approved and they didn't have to present the kind of data or trials where the things we're talking about today would have possibly been picked up or followed, like they went through a process -- which, again, my understanding is that it's a Level II process. If there's something already out there that you're just like, you can go through a process where you don't have to show as much information, whereas if you do a PMA, you've got to show the trials and all the safety, and it's much more an intensive process that, in my limited understanding, includes looking at all of these things before you actually approve the device.

So you might say to the device maker, okay, here are all the things that you've got to think about. You brought this idea for this device to us. Here are the things we want you to look at, and we're going to say to you, you must bring us animal data about the safety, you must bring us an engineered-type non-clinical model about the dissemination of particles. And the company goes and does that and then brings the results back to you. And then you decide whether to approve it. Because my understanding is that the Level II process just doesn't include all of that, what we're talking about right now, but I'm sure I'm not correct.

DR. DIAMOND: So can I just ask a question which might be helpful? It's my understanding that FDA, at times, will require clinical trials as part -- for a Class II product and that not all Class III products would come to a Panel; sometimes FDA looks at them on its own. Are both those comments correct?

MS. BLYSKUN: Elaine Blyskun, that's correct.

DR. DIAMOND: Okay. Thank you.

Did one of you have a comment? Otherwise, I'll go to Dr. Talamini. Elaine, did you have a question, Dr. Blyskun?

MS. BLYSKUN: Yeah. I just kind of wanted to drill down a little bit more with you, Dr. Brown, if that's okay. So what about the bag would you have liked to have seen if you -- if we could take a step back?

DR. CAROL BROWN: So I guess I got myself confused. I wasn't

saying that I had a lot of concerns about the bag, but when -- I can't remember who mentioned this issue of the bags possibly injuring things or when you collapse them, they grab things. The reason I brought up the Level II is that the bags are already out there, so they can be used now. And so if you're talking about adding an indication, I guess, for the bags to be used in conjunction with the power morcellator, then you would have to be saying to them, in order to test these issues, since they weren't tested before, you'd have to have some mechanism for saying to the company/manufacturer, even though you already have this product out there and you could just start using it with the power morcellator, you've got to bring us some evidence that it addresses the safety. That's all I mean. Forget the labels I'm putting on it, but that's the information.

DR. DIAMOND: Okay. Dr. Talamini?

DR. TALAMINI: So this is Talamini. Two points. One, the bags that we have and the grinders that we have are what they are, and we know they have problems. I think for innovation to occur, whatever somebody comes up with is going to need to be different enough to move away from those models, that it's unlikely to be a predicate device type of a pathway, or it's unlikely to be satisfied by -- it's not likely to be close to what we already have if it's going to be that much better, if that makes any sense.

The second point is, in terms of this specific issue of disseminating unsuspected tumor, we won't be able to answer that question

in a human trial in this model. It's only going to be answered on a bench or in an animal model, in my view.

DR. DIAMOND: And just a point of clarification for what Dr. Talamini was trying to say, correct me if I'm wrong, but if there is no predicate device, then you would not be able to use a 510(k) mechanism is what you were saying, but without having said that?

DR. TALAMINI: Well, I don't want to be that specific. This is Talamini again. What I'm trying to say is that we've got what we've got. For something to come along and be better enough to address this problem, it's going to have to be different than what we have, substantially different than what we have, I believe. And that's why my colleague here is using the word containment device instead of bag, I think.

DR. DIAMOND: Okay. Dr. Isaacson?

DR. ISAACSON: I think this would be a process, and it's going to be an exciting process, to first start at the bench, and let's decide, number one, do we need to contain cells, do we need to contain chips, is there a certain micron size that is important, as well as we can look at the actual number of cells which are important, or is it just spilling of one cell. So that's a place to start.

Once you do that and you have that information, then again, on the bench, you can determine if your containment system is adequate to contain that number of cells and that size of cells. And then once your

containment system has addressed that and the company is satisfied and met that criteria, then you go to the animal testing in which you, again, simulate the best that you can the clinical scenario, where you have the bowel and you have the blood vessels and you have the pneumoperitoneum and everything that you can.

So this is clearly not an either/or. This is a unique, really good opportunity to start at the basic level. What's the number of cells? What's the size of the cells? What's the size of tissue that's clinically important, and then work your way up from there. And I think this can be done in a -- without being too burdensome to whoever is going to take this on.

DR. DIAMOND: Okay. Dr. Wentzensen?

DR. WENTZENSEN: I still think that clinical data will be important. It doesn't need to be coming from trials necessarily, and it's going to be very hard to get at those endpoints. But you can probably come up with some clinical phase of a study where you just measure the spread of any tissue, because that will be a surrogate of what's happening in the worst-case scenario. So I think that there must be ways to also -- I wouldn't rely on animal studies and then making those recommendations.

DR. DIAMOND: Okay. Dr. Snyder, did you have a comment? No? Okay. Dr. Iglesia?

DR. IGLESIA: Cheryl Iglesia. Yeah, I really think that clinical data is important. You know, I think that the in vitro bench stuff is helpful,

obviously, in innovation. And the lab-ing would be useful in safety and the guidance that we clearly need. But the clinical data doesn't necessarily have to come from randomized trials which are not feasible. Clinical data can come through postmarket surveillance of these new bags and potentially new devices or clinical registries. And that's where you get your comparators.

And that's why I was asking how is the best registry, because what about the people who are getting uterine fibroid embolization and they have a leiomyosarcomas undiagnosed and delayed in diagnosis that has a bad outcome? What about the people who are getting manually morcellated? There is an issue. It's not just the power morcellation. What about the people getting the radiofrequency? It's not in there yet, but probably not in short order that radiofrequency is going to be radiofrequency through some tumor.

And I feel very strongly about that. That would be a way of not hindering innovation, but at least we can see signals earlier because the MDR is not accurate, you know? Not everybody reports it. It's voluntary. You get people like Amy Reed and Dr. Noorchashm, who were very vocal, and gratefully so, you know, put that on there. But I think that would be a really big step for women's health.

DR. DIAMOND: Dr. Corrado?

DR. CAREY-CORRADO: Yeah. I'm going to ask if Dr. Iglesia can again outline maybe more specifically. So this would be a postmarket clinical

data collection effort and --

DR. IGLESIA: On how these bags are performing in vivo.

DR. CAREY-CORRADO: Okay.

DR. IGLESIA: How are these bags performing? Are there certain surgeons who have a higher rate of vessel injury, bowel injury, other non-target injury, you know, are they not following the guidelines --

DR. CAREY-CORRADO: So it's the bag -- it's the combination of the bag plus --

DR. IGLESIA: It's a combination of patient --

DR. CAREY-CORRADO: -- a power morcellator?

DR. IGLESIA: But I think a registry for how we're treating uterine pathology is necessary.

DR. CAREY-CORRADO: So that's probably a different data collection effort, though.

DR. IGLESIA: And that's why I was thinking about the comparators.

DR. CAREY-CORRADO: Okay.

DR. IGLESIA: But in this particular scenario, you know, it's how are we treating fibroids and the undiagnosed, and I don't think it's necessarily just power morcellation. I think morcellation or the way you extract the tissue is really important because it gets back to making the -- not doing it in high-risk patients.

DR. CAREY-CORRADO: So the only follow-up I would have, and maybe it's just me is that, for our purposes, for the immediate purposes of this clinical problem, would you agree that your first priority would be evaluating a bag or some kind of containment system plus a power morcellator to see how they are performing? And then this other effort, you know, more broadly looking at how are people managing fibroids, you know, with procedures, and what is the risk of, you know, encountering the same type of morbidity and mortality possibly as a sequel of one of these other procedures. Am I getting that --

DR. IGLESIA: I agree that it's a start, but it's just the tip of the iceberg.

DR. CAREY-CORRADO: Okay.

DR. CAROL BROWN: Carol Brown. Sorry to belabor this. So I just want to clarify that I think as a GYN oncologist and a cancer scientist, that, in order to address numbers one and two, you don't need a clinical trial. In fact, it's never going to be feasible. In fact, we don't -- throughout this whole process, the goal is to stop using morcellators and make more awareness in women who are at high risk. But we want to come out of this for a device that we can use comfortably in women who this is a great advantage and that whatever containment device, you know, the reason this happens is because some cells are getting out of the containment.

So I think what you have to show, and I don't -- you can --

never going to show this on a clinical trial because the endpoint, leiomyosarcoma, endometrial sarcoma, everything is so rare that even a postmarket -- it would take 15, 20 years. And, hopefully, you would never see it again because nobody will ever use it again when they shouldn't. I think that you just need to prove that the particles aren't getting out, but in terms of the safety things, I think you do.

But then my question would be, so let's say somebody comes up with a new morcellator that includes a containment device. And, again, I'm getting away from the bags, because the bags are already out there, and if we go by what you're saying, are you saying that now the FDA needs to do a postmarket analysis and the bags are already out there? I don't think that's what we're saying. But if there's a new device, I personally don't think -- does the company -- and if it works electrically the same way the other devices have worked electrically that are similar that you already know are safe, do they actually have to do a clinical study to show it's safe electrically, or do they need to do the clinical study just to show that -- or the simulation study to show that it doesn't damage vessels, or whatever.

I just think -- is there some leeway in that? I mean, are you able to look at different parts of the device as to what already exists and you know is safe versus the parts that are really new?

DR. CAREY-CORRADO: Yeah. And that's the fundamental impetus of the 510(k) process, just to look at those parts that are new or

different. I mean, consider it all in its entirety, but we don't have to test everything in the clinic. We can do some on the bench because we know how to do that or we can figure out bench methods.

I would suggest, you know, these are not mutually exclusive, as I think Dr. Isaacson was talking -- it would be a progression. I mean, there is no way we would even allow, even if we all agreed in this room that a clinical study was necessary, we'd never allow it to go into a patient until they did bench testing. So we're going to get, okay, the bench testing, animal and/or clinical.

DR. DIAMOND: Dr. Fisher?

DR. FISHER: Thank you. So with those points of clarification, okay, this is really meant to be a discussion among yourselves. So I would like to kind of step back a little bit if you need some clarification and go ahead and return the discussion to the Panel if we can.

DR. DIAMOND: Okay. So, Dr. Iglesia, you mentioned before that the items that you'd already discussed were just the tip of the iceberg. What other criteria would you like to see addressed in such a study?

DR. IGLESIA: You know, I like -- I want data that we can use to best inform our patients --

DR. DIAMOND: So what are those endpoints? What specifically would be looked at?

DR. IGLESIA: Now, what are we talking about --

DR. DIAMOND: What sort of guidance can we as a Panel --

DR. IGLESIA: For hysterectomy, for power morcellator used, for treatment --

DR. DIAMOND: For either one.

DR. IGLESIA: So I'm looking at this very globally in terms of women who are diagnosed with uterine fibroids, you know?

DR. DIAMOND: Um-hum.

DR. IGLESIA: And we're talking to them and counseling them about different and various treatment options. And they want to know, Doctor, what do you think I should do, or what do you think is my best choice? You know what? I'm worried about cancer, and what is my risk of having cancer given my profile? And what happens if I don't do anything? Is there a role for medical management? Can we just remove the fibroid safely? Is that safe to use? Do I need a full hysterectomy? Now, what is the best route of hysterectomy? And those are the kinds of discussions that we need to be informed with data that, you know, we have very limited follow-up on many of the modalities that we use for women.

And we have non-precise preoperative diagnosis for a condition that is extremely common and affects up to 80% of people. Now, granted, only a small -- 80% of women. Only a small proportion end up being symptomatic, and it's, you know, only a small proportion have, what are we saying, 600,000 end up having hysterectomies, and 40% of those have -- are

done for fibroids. And it's even rarer to have a cancer from that. But, you know, I think that all these different treatment modalities and what the long-term follow-up is we don't have a lot of data for.

DR. DIAMOND: Dr. Shriver?

DR. SHRIVER: In order to drive the innovation, you've got to withdraw the accreditation of the present devices. And then here is industry, who are going to say, okay, what they want is certainty, I think, as the way forward. What's the certain way forward? It's get into the lab. It's devise the next generation device. And then do clinical testing. I think you're underestimating the ability of these huge gynecologic societies, hundreds of thousands of patients undergoing the procedures now, to enroll in clinical trials. I mean, these concerns have been brought up before in the 1990s, when high-dose chemotherapy in bone marrow transplant was being used off of clinical trial, and there was concerns raised as to whether it was effective or not. And, finally, the government said, okay, we're not going to do it that way anymore. In fact, the insurance companies said you got to be on a clinical trial for this. And people complained and this and that. At the end of the day, the randomized controlled trials of tens of thousands of women, because it's a very common diagnosis and procedure, showed that there was no difference. In fact, there was harm being done. We don't do autologous bone marrow transplant for breast cancer anymore, and that's why.

So I think you're underestimating the fact that in a procedure

that's done as often as this that it can't be done. Yes, it can be done. What's the signal? Well, you have primary and secondary outcomes for any clinical trial. Of course, the primary one is, you know, how much leiomyosarcoma is there. But the secondary outcomes are ones that you develop in the lab or the animal model. You test the containment device after use for leakage, for breach. I mean, to use the bag terminology, you pull it out of the abdomen, and there's something that goes on off the OR table where you just fill it with colored water and see it if leaks. I mean something as simple as that. I don't mean to say it's that simple, but you test the integrity of the devices. And then if the secondary endpoints are reached and things are good after, I mean, 10,000 patients, then the trial is stopped because it's showing equivalency.

But with no devices approved, you think industry is going to turn their backs on this huge patient population, this huge need apparently by gynecologists to have this type of technology? Because the first one who gets this approval and gets it to market will be the only ones who have the device. And so I think you're underestimating the fact that it can't be done with secondary outcomes, that you underestimate the need of both physicians and surgeons and the patients, and they will enroll. And in cancer, tens of thousands of patients in clinical trials is not unheard of, and it's commonly done.

DR. DIAMOND: All right. I'm not seeing any additional

comments or advice from the members of the Panel. So, Dr. Fisher, Dr. Yustein, have you gotten the answer that you need for this question?

Yes?

DR. PRICE: May I just ask maybe Dr. Isaacson, any idea for an animal model if that were to be a step in the test process?

DR. ISAACSON: Well, certainly you'd want a -- I would suspect a larger animal model. Whether it's going to be a porcine model or a goat or something like that -- go ahead.

DR. TALAMINI: So this is Talamini. So in the era where we had great concerns about port site recurrence in the laparoscopic treatment of colon cancers, there was a lot of biology work done that you can find in the literature from the early '90s. And it was largely in pig models, but also in some mouse and rat models. And it was fairly well developed in that era and well described and could potentially be a model for this.

DR. ISAACSON: I think most of those smaller animal models probably now could be done with bench testing in a lot of those same things. And it's not until you're trying to recreate the human anatomy the best you can that you get into the larger animal models.

DR. DIAMOND: Dr. Brown?

DR. CAROL BROWN: I would just like to have a pause and remind ourselves that, you know, it's 2014. We now have amazing simulations for human anatomy that I would think, you know, animal -- using

animals in research is a whole 'nother meeting, but I do think there is a general agreement we want -- and I think the government is interested in limiting it unless it's really necessary. It's hard for me to imagine why it would be necessary to test things like the anatomy issues to use an animal model because companies have amazing simulators for everything that we do in a human being that are -- that you could use for all the things about injuring a vessel, pulling in a piece of bowel. I mean, they exist now in our laparoscopic training simulators that are just like a human being.

So I think you want to just be cautious and really -- and, again, this will be up to the innovators to decide where do they really need to use a living animal to -- what do you really need a living animal to test? I don't think you're going to need a living animal to test injuring bowel, bladder, electrical shock. That can all be simulated with, you know, a human robot kind of thing.

DR. DIAMOND: Dr. Fisher?

DR. FISHER: Yes. I just wanted to say that we're very aware of the Tox21 Initiative, and so we don't take the use of animals lightly, so --

DR. DIAMOND: Other additional points the FDA would like to have clarification on or advice on, on this question?

(No response.)

DR. YUSTEIN: Dr. Diamond, were you going to just summarize the Panel's recommendations for that last set?

DR. DIAMOND: I could try. So with regard to Question 9, the consensus that I thought I heard around the table is that the list of identified risks is a complete list. The mitigation measures, there were some thoughts that there may be a need for -- well, the mitigation measures that FDA has suggested, by and large, appear to be adequate, and the ones that would need to be done, that there may be a place in specific examples for either simulators or large animal studies for, particularly, I guess, the first three or four risks that were identified, and that there were no other mitigations that were, I don't think, suggested.

Clinical data, there was thoughts that there needed to be -- it would be helpful to have comparators for power morcellators with other forms of morcellation or other methods of treatment of uterine fibroids. And there was some discussion as to whether some of that might be in the form of postmarketing studies or in descriptions of clinical use, current clinical use.

Does anyone from the Panel have additions to that?

DR. YUSTEIN: So if I can make one comment, and I guess this is talking to a little bit of what Dr. Iglesia was saying and what you were mentioning, AHRQ will be setting up a registry. They're working for PCORI, the Patient-Centered Outcomes Research Institute. And in September, they posted a request, an RFA, for the development of a prospective, multi-center, practice-based clinical registry for looking at patient-centered outcomes for the treatment of uterine fibroids.

They will be looking at all types of options, including uterine artery embolization, MRgFUS, radiofrequency ablation, et cetera, in women of childbearing age specifically. Patients undergoing hysterectomy and myomectomy will be included in that registry, although the percentage of patients in that registry will be limited to I think about 25% maximum that have had hysterectomy.

So, unfortunately, Dr. Berlinger, who is from AHRQ, was going to be here these past couple days -- I think she was here yesterday, and I don't think she's here today -- Dr. Diamond, is it okay if I ask in the audience if Dr. Berliner --

DR. DIAMOND: Sure.

DR. YUSTEIN: Is Dr. Berliner here by chance?

(No response.)

DR. YUSTEIN: Unfortunately, she might have been here earlier. And she, you know, certainly, they have this RFA out, and it wasn't designed to look at the morcellator issue. But, certainly, if the professional societies and other organizations would want to look at joining up with AHRQ and PCORI to work together to see if the registry can be modified in some way that might help us figure it out, I think they would be open. I can't speak for AHRQ, but they might be open to at least having those discussions.

So I think that there is something coming down the road. Whether or not it can or can't answer those questions that you proposed,

Dr. Iglesia, there is some kind of registry that AHRQ is looking to to set up. And that will be -- it won't be a national registry. I think it's going to be looking at 10 or 12 large clinical sites. But, again, it will be -- it will provide some comparator. But, again, mostly focused on effectiveness comparisons between outcomes, but they will also be collecting safety data.

DR. IGLESIA: Any opportunity to test morcellation would be excellent.

DR. YUSTEIN: Again, I think it would be outcomes rather than the actual testing of the device, yeah.

DR. DIAMOND: Yeah. I think in view of all the discussion this topic has generated, I would be very surprised if the registry they do would not include information relevant, very relevant to this topic.

DR. YUSTEIN: I think they didn't think they were going to have the power to -- because of the limitation of the patients undergoing hysterectomy, the restriction on that, that they were going to have the power to necessarily look at all the endpoints that might be relevant to this issue.

DR. DIAMOND: And with some of the numbers that we've heard, that may very well be true, but nonetheless, I think they would like to -- it would surprise me greatly if they would not try to collect as much information as they could as related to this very important topic.

DR. IGLESIA: But what's more important about that --

Cheryl Iglesia -- is that, you know, not only is it a registry of clinical outcomes, objective outcomes that -- you know, PCORI stands for patient-centered outcomes. And, you know, it is my belief that, you know, that trumps, you know, what we think is important, you know, what the patient is feeling, what the patient experiences. So that's what's very important about that registry.

DR. DIAMOND: All right. So any other comments from the Panel? If not, I'm going to read a -- yes, Ms. Aronson?

MS. ARONSON: I just sort of have a wish. It's not been in our purview to talk about this, but my hope is that somehow the patient organizations or some entities/societies start looking into cause. You know, are there clusters, are there environmental factors, you know, and all this will help understand the issue even more. Thank you.

DR. DIAMOND: Thank you.

All right. Then I would like to thank the Panel and the FDA for their contributions. I would also like to thank all of the Open Public Hearing speakers, the medical professional societies, and the patient advocacy and research organizations for their remarks.

Dr. Yustein or Dr. Fisher, do you have any final comments or remarks you'd like to make?

DR. FISHER: I just have a quick summation, if I could.

DR. DIAMOND: Please.

DR. FISHER: Okay. I promise I won't take too long here to sum up these two days. So over the past two days, we've heard testimony and presentations from the medical professional societies as well as industry, patient advocacy groups, research organizations, the general public, as well as the invited FDA speakers.

If the issue that was on the table was just morcellation of a truly benign tissue, none of us would be here today. I think one of the major challenges that we're facing is identifying the uterine sarcoma prior to any procedure. Now, when you look at risk, we talk about rate and we talk about severity. And we've talked about a lot of different numbers over the past two days, 1 to 350, 1 to 7,000. And although we may not agree on the actual number, I think it's very encouraging that there's a number of parties that are already working in this area. It's been said that we should really look at this further because this is an important part to helping to inform not only the patient but the physician. But regardless of the rate, when we talk about risk, we also have to talk about severity. And regardless of the rate, we know that the severity of spreading an unsuspected cancer is great.

And we've talked about risk mitigation strategies. We've talked a little bit about trying to identify low-risk populations. One of the things that we talked about was imaging. Is this a possible modality that in the future will improve to a point where we're actually able to discriminate or to tell the difference between a fibroid and an LMS?

The one thing that we don't want to do, FDA does not want to put forward a front that's going to discourage technical innovation. So, hopefully, I got my point across when we were talking about bags. I'd like to expand that out to a containment device because I think we're open to innovation, and we want to encourage that.

We also talked about education along a lot of different ways. We talked about education for the patient. What information do we have to have that the patient needs? And I think that there's also information that we have to have that the patient needs. And in additional to that, Dr. Levy gave a presentation today on possible training that could be put out there for physicians also. So I think that there's a lot of opportunities here.

So that's a big task. I'd like to go back to a comment that Dr. Yustein made this morning. And on one of his slides, he says that FDA recognizes limitations of available data and agrees that more data -- that more quality data is always better. So I agree with that. The question is who is responsible for generating all this quality data? And my answer to that would be everybody in this room. I mean, FDA can do so much. But I think, really, what we're looking for is to help with the professional societies, the patient advocacy groups, the patients themselves, the general public. I think everybody has a responsibility and has a right to be heard on these issues.

So Dr. Simon yesterday asked me, or asked us, has FDA learned from any previous experiences and what could you carry forward? And the

example that I gave was the work that we had done on latex. And I think that the issue with latex was that there was a delay or hesitation in even acknowledging that there was an issue. In this situation, when we're talking about the morcellation of uterine fibroids, I think we would all agree that there's an increased awareness and an acknowledgement that there's a real public health issue here. And I hope that, based on the actions that FDA has taken thus far, that everybody realizes that FDA considers this to be a high priority issue.

So, in moving forward, we're going to take into consideration all information that has been shared at this meeting and any other data that is or becomes available to us. I'd like to remind everybody that the docket is still open for the next couple weeks. So we will continue to collect information that's provided into the docket. And I'd also like to make it clear that, of course, any next steps that we take will be publicly communicated.

So, with that, I would like to thank everybody for their participation over these last two days. It's been long, but I appreciate everybody hanging in there. My thanks to the Panel, who's traveled very far to be here, to the professional organizations, to the patient advocacy groups for your participation and for your involvement in this, and last but not least, I would actually like to applaud the fortitude of the families that came forward with their testimony because it was hard on them, I know, but it was important to us. So thank you very much.

DR. DIAMOND: All right. The July 10th and 11th meeting of the Obstetrics and Gynecology Devices Panel is now adjourned.

(Whereupon, at 5:00 p.m., the meeting was adjourned.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

OBSTETRICS AND GYNECOLOGY DEVICES PANEL

July 11, 2014

Silver Spring, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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